XELJANZ® (tofacitinib) for the Treatment of Psoriatic Arthritis (PsA)

Arthritis Advisory Committee (AAC)

August 3, 2017

FDA White Oak Campus

Silver Spring, MD

Introduction

Nancy McKay

Director, Regulatory Affairs

Pfizer Inc

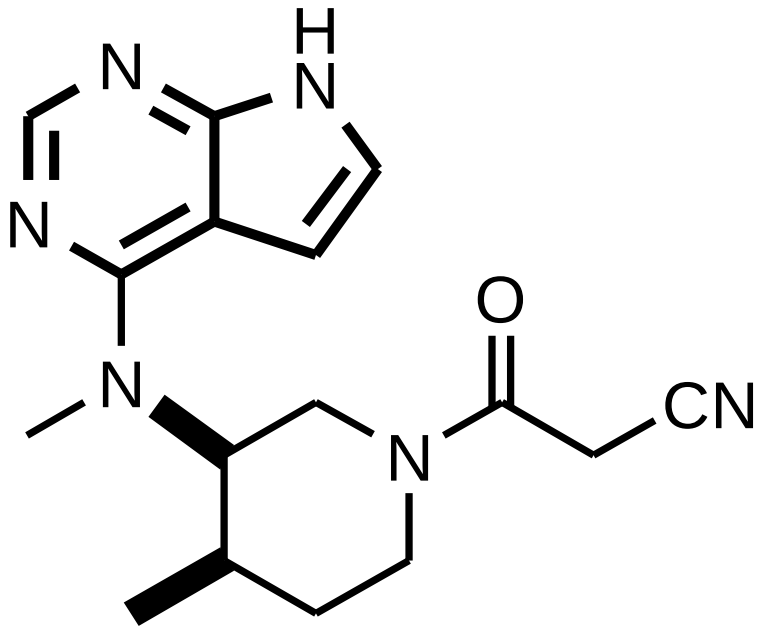
Overview of Presentation

Topic	Presenter
Introduction	Nancy McKay Director, Regulatory Affairs Pfizer Inc
Psoriatic Arthritis: A Physician's Perspective/ Unmet Medical Need	Philip Mease, MD, MACR Director, Rheumatology Research, Swedish-Providence-St. Joseph Health Systems Clinical Professor, University of Washington School of Medicine, Seattle, WA
Tofacitinib PsA Development Program and Efficacy	Keith Kanik, MD, FACR Senior Director, Global Clinical Lead PsA Inflammation and Immunology Pfizer Inc
Tofacitinib PsA Safety	Daniela Graham, MD Clinician, PsA Development Program Inflammation and Immunology Pfizer Inc
Risk Management	Thomas Jones, MD Senior Director, Safety Risk Management Pfizer Inc
Benefit:Risk and Conclusions	Michael Corbo, PhD Senior VP, Chief Development Officer Inflammation and Immunology Pfizer Inc

Tofacitinib is an Oral, Small Molecule JAK Inhibitor

- JAK inhibition is partial and reversible and interferes with signaling of cytokines important in psoriatic arthritis
- Effective oral drug with manageable safety profile and efficacy similar to TNF-inhibitors
- Provides an oral option to address unmet needs for the treatment of patients with active PsA

Tofacitinib



Flanagan ME et al, *J Med Chem* 2010; 53:8468-8484.
JAK=Janus Kinase; TNF=Tumor Necrosis Factor

XELJANZ® (tofacitinib) Development Program and Clinical Experience

- Xeljanz studied extensively with Phase 3 clinical development programs
  - Including rheumatoid arthritis, psoriasis, psoriatic arthritis, and ulcerative colitis
- Cumulatively, 22,132 patients have participated in the tofacitinib clinical development program with patients exposed for up to 9 years
- The total estimated post-marketing exposure is in excess of 83,000 patient-years (PY)
- The safety of tofacitinib for the treatment of PsA is based on a clinical development program that consists of
  - 783 PsA patients that have been exposed to tofacitinib
  - 775 patient-years of tofacitinib exposure as of May 10, 2016

XELJANZ® (tofacitinib) Regulatory History

- Rheumatoid Arthritis (RA)
  - Adult RA 5 mg BID IR NDA Approved – November 6, 2012
  - Adult RA 11 mg QD XR NDA Approved – February 23, 2016
  - Tofacitinib tablets are approved for RA in more than 80 countries; including US, Canada, EU countries and Japan
- Other Indications
  - PsO sNDA CRL – October 9, 2015 / sNDA Withdrawn – July 26, 2016
  - PsA sNDAs (IR and XR) Submitted – February 22, 2017
  - UC sNDA Submitted – May 4, 2017

BID=twice daily; CRL=Complete Response Letter; IR=Immediate Release; mg=milligram; NDA=New Drug Application; PsO=Psoriasis; QD=once daily; sNDA=supplemental New Drug Application; UC=Ulcerative Colitis; XR=Extended Release

Tofacitinib for the Treatment of PsA

- 5 mg BID of tofacitinib in PsA has shown efficacy consistent with bDMARDs in TNFi-naïve patients, while also demonstrating similar efficacy in TNFi-Inadequate Responders (IR)

- The safety profile of tofacitinib, including that in PsA patients, is well characterized, stable and manageable. It is informed by a large and growing safety database, with consistency between real world and clinical safety data

- The benefit:risk profile of tofacitinib 5 mg BID for PsA is positive and is based on substantial clinical evidence

bDMARD=biologic Disease-Modifying Anti-Rheumatic Drug; TNFi=Tumor Necrosis Factor inhibitor

XELJANZ® (tofacitinib) for PsA
Proposed USPI: Indication and Dosage

Proposed Indication in sNDA
(1. INDICATIONS AND USAGE)

XELJANZ is indicated for the treatment of adult patients with active psoriatic arthritis

Proposed Dosage in sNDA
(2. DOSAGE AND ADMINISTRATION)

The recommended dose of XELJANZ is 5 mg twice daily used in combination with conventional synthetic DMARDs

USPI=United States Package Insert

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Psoriatic Arthritis: A Physician's Perspective/ Unmet Medical Need

Philip Mease, MD, MACR

Director, Rheumatology Research, Swedish-Providence-St. Joseph Health Systems

Clinical Professor of Medicine, University of Washington School of Medicine, Seattle, WA

Disclosures for Philip Mease

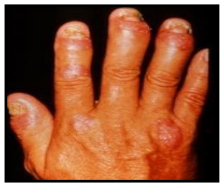
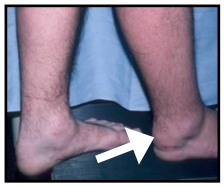
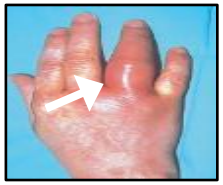
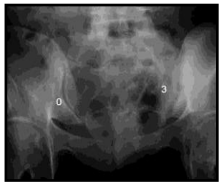
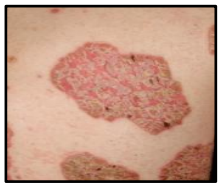
- Research grants, consultation fees, and/or speaker honoraria: Abbvie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Crescendo, Genentech, Janssen, Lilly, Merck, Novartis, Pfizer, SUN, UCB

Professor Mease: Relevant Clinical, Research, and Education Experience

- **Clinical Practice**
  - Clinical rheumatologist for 35 years and Clinical Professor, University of Washington, Seattle
  - Clinical experience with tofacitinib in RA patients since approval in November 2012
- **Research experience**
  - Conducted the first trial of TNFi therapy in PsA and participated in most PsA development programs
  - Involvement in tofacitinib RA studies and in tofacitinib PsA clinical trial design and data interpretation
- **Relevant committees and working groups**
  - Founder and current executive committee member of Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA)
  - OMERACT PsA working group, the National Psoriasis Foundation PsA task force, and ACR-NPF PsA treatment recommendations working group
  - Scientific director, Corrona PsA-SpA registry

ACR=American College of Rheumatology; OMERACT=Outcome Measures in Rheumatology; NPF=National Psoriasis Foundation; SpA=Spondyloarthritis

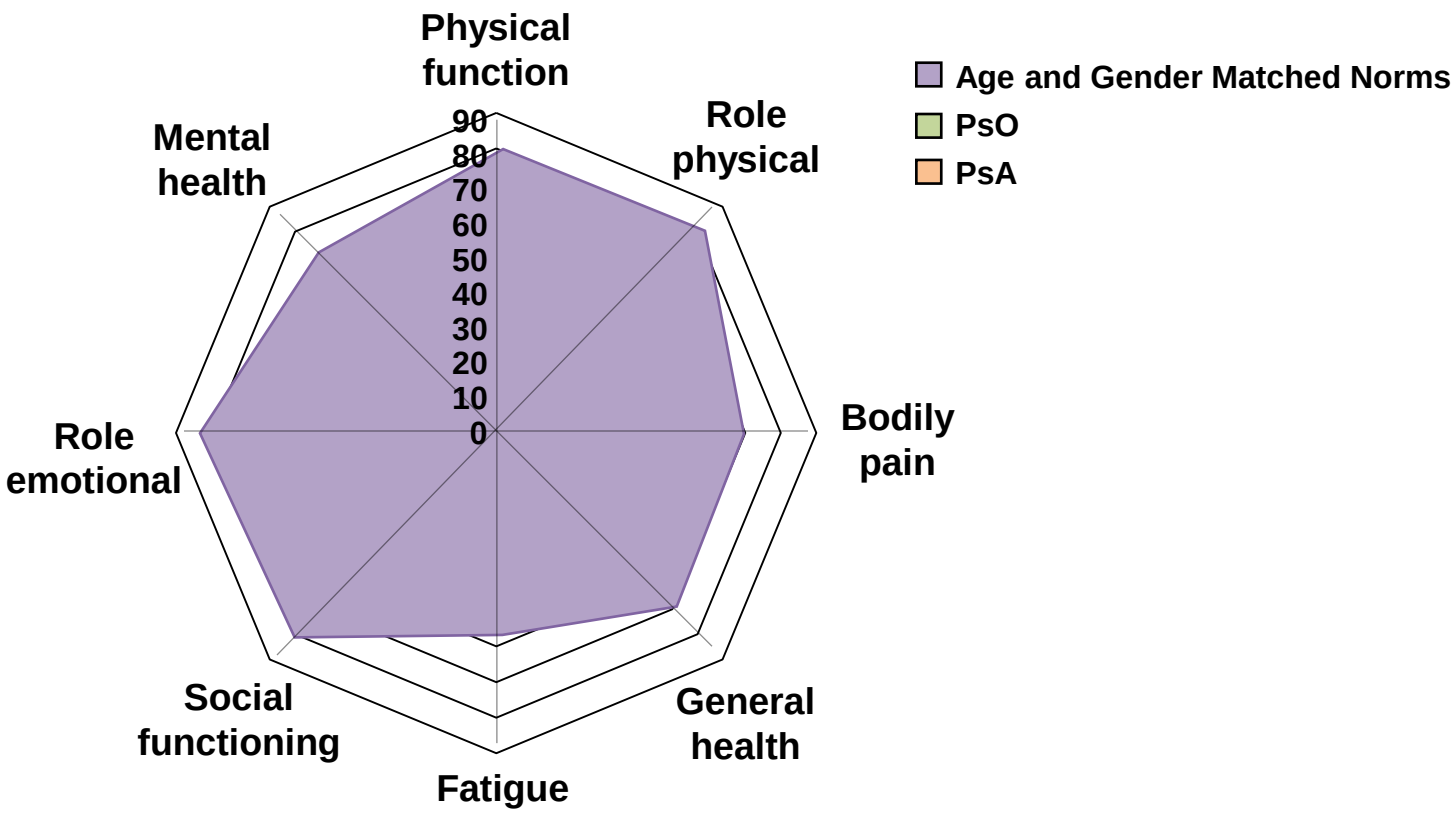
Psoriatic Arthritis is a Distinct Disease Encompassing Numerous Clinical Manifestations[1]

Peripheral Arthritis		■ Arthritis affecting joints such as those in hands, feet and knees ■ Progressive disability and joint destruction may occur
Enthesitis		■ Enthesitis is inflammation where tendons and ligaments attach to bone. Enthesitis can occur virtually anywhere in the body. It often appears at the insertion of the Achilles tendon or plantar fascia in the heel, causing walking and standing disability
Dactylitis		■ Dactylitis is significant swelling in the fingers and toes, creating a sausage-like appearance. This is painful and causes stiffness and disability
Spondylitis		■ Psoriatic arthritis in the spine and sacroiliac joints is called psoriatic spondylitis. This results in back pain, stiffness, inability to move and work impairment
Skin Psoriasis		■ Psoriasis causes red, scaly, itchy, raised patches on the skin

1. Ritchlin C et al. *N Engl J Med* 2017;376:957-70.

PsA Impacts Patient's Health Related Quality of Life, Physical and Mental Health

Comparison of Health-Related QoL in PsA and PsO using the SF-36



Strand V et al. *Ann Rheum Dis* 2012;71:1143-1150.
QoL=Quality of Life; SF-36=Short-Form 36-question Health Survey

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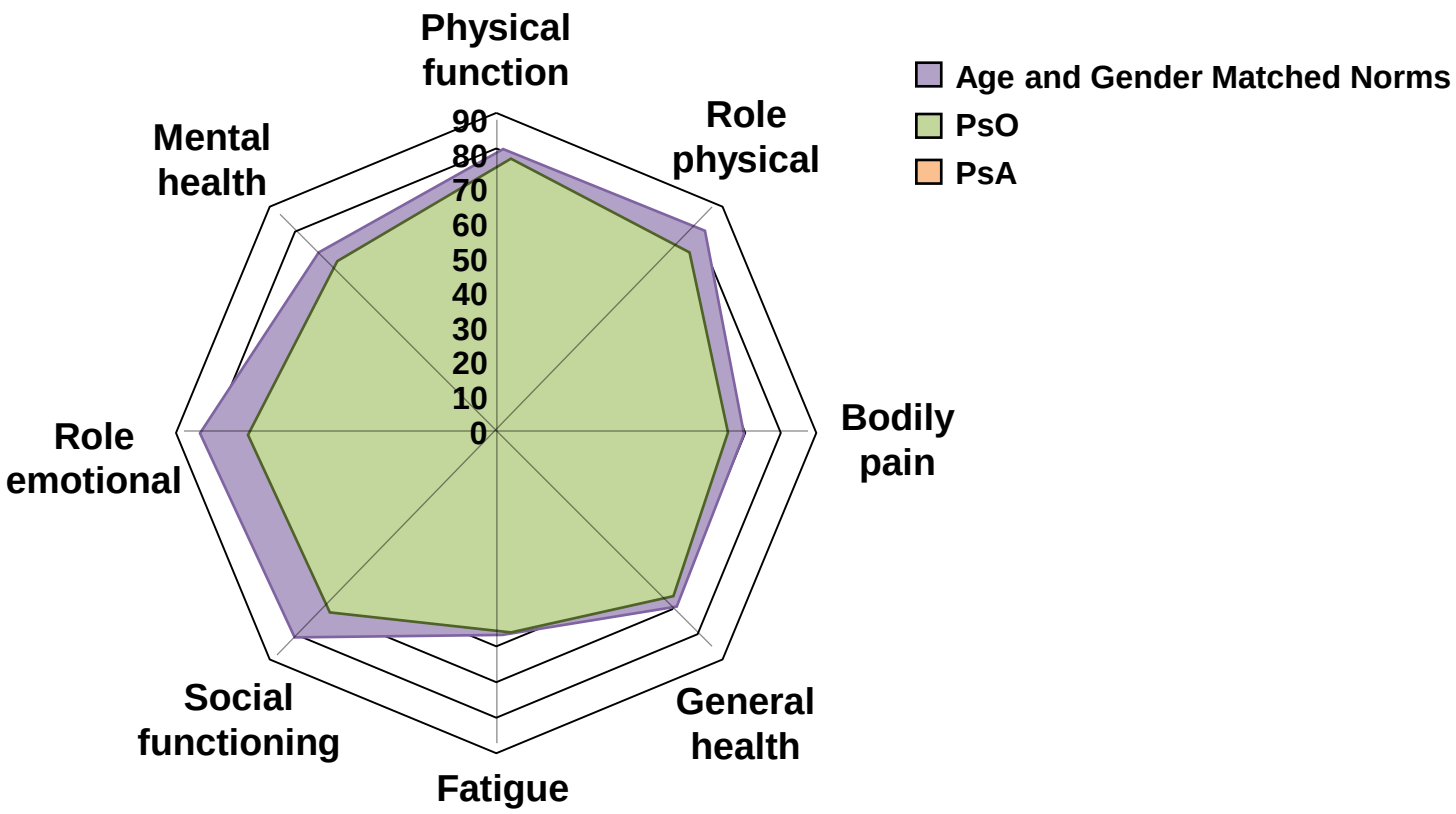

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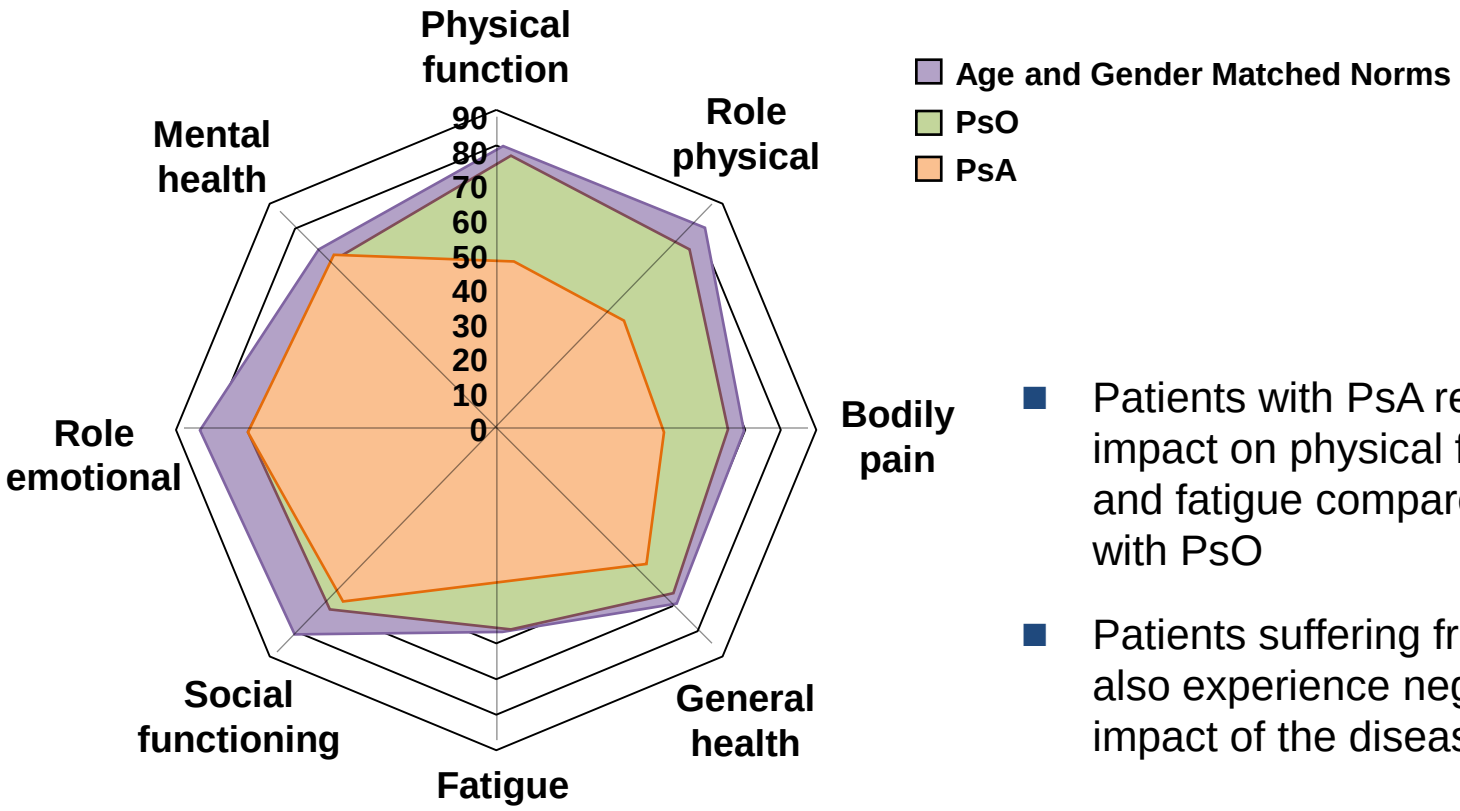

- Patients with PsA reported greater impact on physical function, pain, and fatigue compared to patients with PsO
- Patients suffering from PsA or PsO also experience negative mental impact of the disease

Health-Related QoL is severely affected in PsA, both for physical and mental health

Strand V et al. *Ann Rheum Dis* 2012;71:1143-1150.
QoL=Quality of Life; SF-36=Short-Form 36-question Health Survey

Existing Therapeutic Options for PsA Have Limitations: A Need for Effective New Therapies Exists[1-5]

NSAIDs and Glucocorticoids	Conventional Synthetic DMARDs	TNF Inhibitors	Non-TNF Inhibitor Biologics	Targeted Synthetic DMARDs
	• Methotrexate • Leflunomide • Sulfasalazine	• Etanercept • Infliximab • Adalimumab • Golimumab • Certolizumab pegol	• Ustekinumab (anti-IL-12/23) • Secukinumab (anti-IL-17A) • Abatacept (inhibits T-cell co-stimulation)	• Apremilast (PDE4 inhibitor)

1. Coates L et al. *Arthirtis and Rheumatology* 2016;68(5):1060-1071.; 2. Gossec L et al. *Ann Rheum Dis* 2016;75:499-510.; 3. Mease P et al. *N Engl J Med* 2015;373:1329-39.; 4. Mease P et al *Ann Rheum Dis* 2017;0:1-9.; 5. Mease PJ. *Ann Rheum Dis* 2011;70(suppl 1):i77-i84.
csDMARD=conventional synthetic Disease-Modifying Anti-Rheumatic Drug; IL=Interleukin; MTX=Methotrexate; NSAID=Nonsteroidal Anti-Inflammatory Drug; PDE4=Phosphodiesterase type 4

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Efficacy csDMARDs

- MTX is one of the most commonly used systemic medications in PsA, yet has demonstrated minimal clinical efficacy for PsA in studies[5]
- MTX and sulfasalazine have little effect on enthesitis, dactylitis, and spondylitis[6]

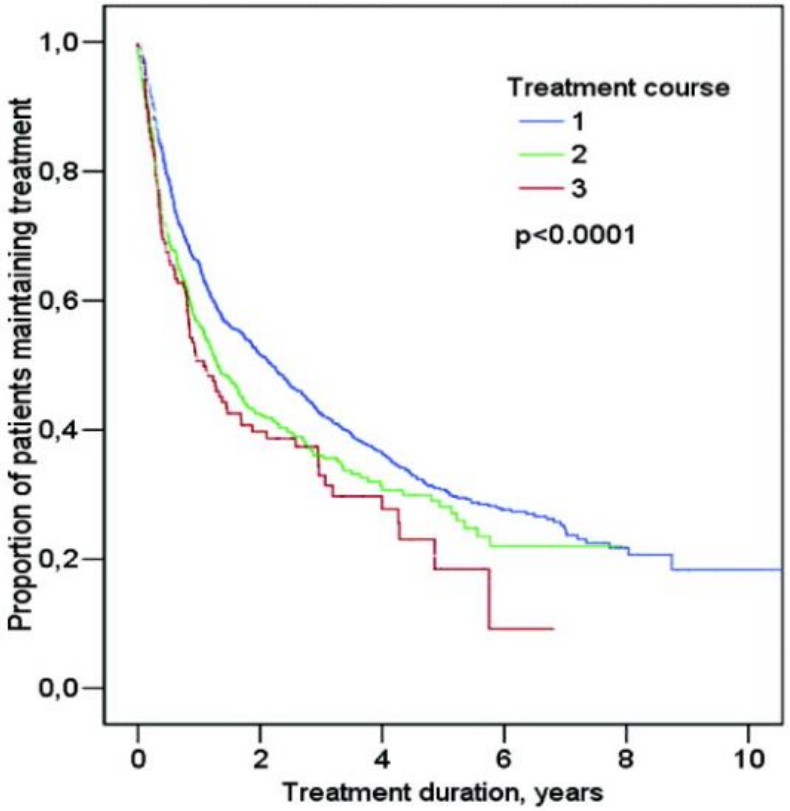
Efficacy of Targeted and Biologic DMARDs

- The goal of achieving low disease activity or remission is now achievable, however
  - 36%-63% of patients do not achieve an ACR20 response at 6 months[7,8-17]
  - 45%-69% may lose response over time or may experience adverse events[8,18]
    - This leads to the need for additional medications to switch[5]

1. Coates L et al. *Arthirtis and Rheumatology* 2016;68(5):1060-1071.; 2. Gossec L et al. *Ann Rheum Dis* 2016;75:499-510.; 3. Mease P et al. *N Engl J Med* 2015;373:1329-39.; 4. Mease P et al *Ann Rheum Dis* 2017;0:1-9.; 5. Mease PJ. *Ann Rheum Dis* 2011;70(suppl 1):i77-i84.; 6. Marchesoni A et al. *J Rheumatol* 2015;93:61-64.; 7. Helliwell P et al. *Arthritis Care Res* 2014;66:1759-1766.; 8. Lebwohl et al. *J Am Acad Dermatol* 2014;70:871-881.; 9. Otezla [package insert]. Summit, NJ: Celgene Corporation; 2014.; 10. Stelara [package insert]. Horsham, PA: Janssen Biotech, Inc.; 2014.; 11. Enbrel [package insert]. Thousand Oaks, CA: Immunex Corporation; 2015.; 12. Simponi [package insert]. Horsham, PA: Janssen Biotech, Inc.; 2015.; 13. Remicade [package insert]. Horsham, PA: Janssen Biotech, Inc.; 2015.; 14. Cosentyx [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; 2016.; 15. Cimzia [package insert]. Smyrna, GA: UCB, Inc.; 2015.; 16. Humira [package insert]. North Chicago, IL: AbbVie Inc.; 2015.; 17. Golmia RP et al. *Rev Bras Reumatol* 2014;54:247-249.; 18. Zhang HF et al. *Arthritis Res Ther* 2014;16:420.

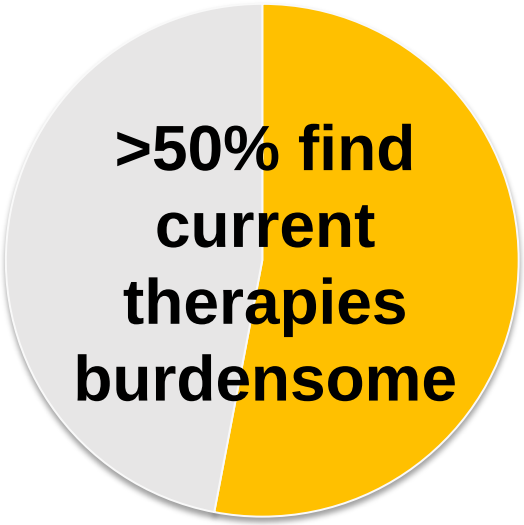
Median Drug Survival in PsA is 2 Years on TNFi

Clinical Response, Drug Survival, and Predictors of Response Among 548 Patients with Psoriatic Arthritis who Switched Tumor Necrosis Factor α Inhibitor Therapy: Results from the Danish Nationwide DANBIO Registry



Glintborg B et al. *Arthritis Rheum* 2013;65(5)1213-1223.
DANBIO=Danish Registry for Biologic Therapies in Rheumatology

Patients Are Dissatisfied with Current Therapies

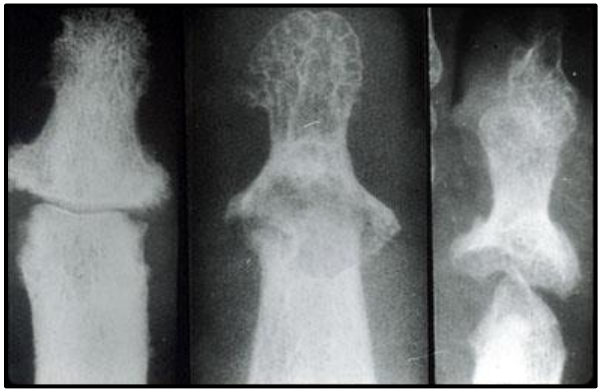


- Several key reasons why treatment was viewed as burdensome were[1,2]
  - Lack/loss of effectiveness
  - Adverse events
  - Fear and anxiety of injections
  - Pain and discomfort of injections
  - Inconvenience

1. Lebwohl M et al. *J Am Acad Dermatol* 2014;70:871-881.
2. Menter A et al. *J Am Acad Dermatol* 2011;65:137-174.

Pathogenic Pathways

Arthritis



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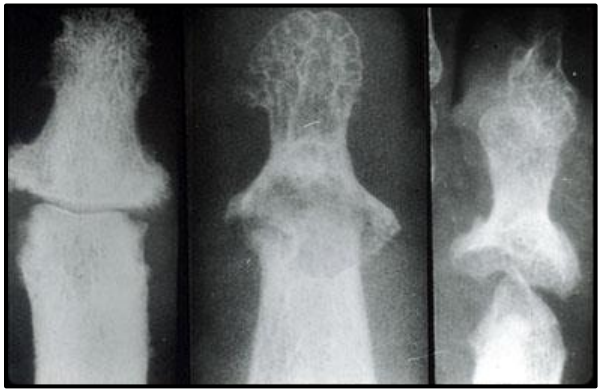
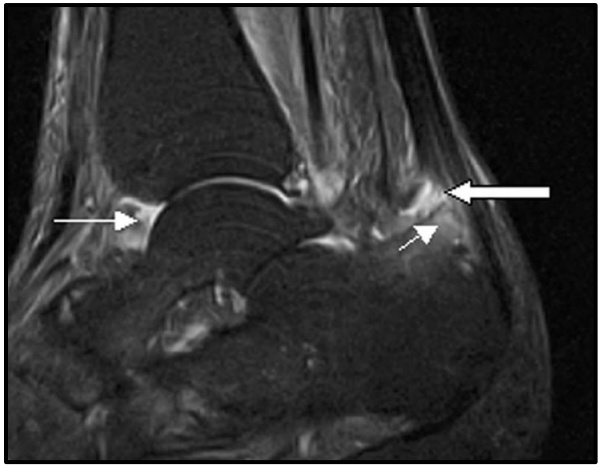


Enthesitis



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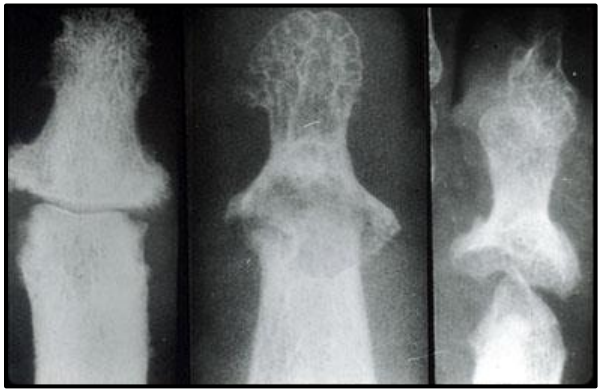

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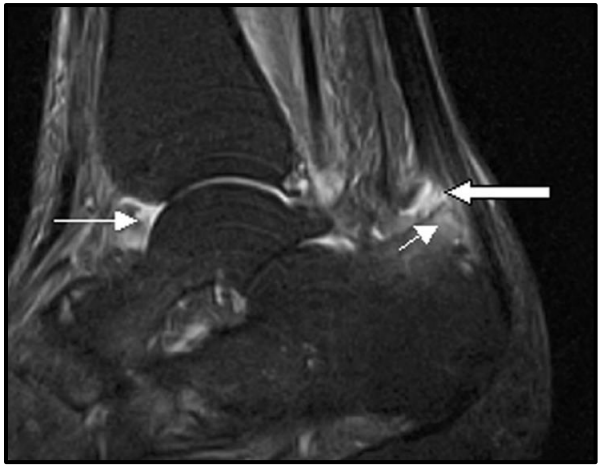

Pathogenic Cytokines are Mediated or Modified by Tofacitinib			
Cell Type	**Function/Physical Signs and Symptoms**	**Activated/ Maintained by Cytokines**	**Produce Cytokines**
CD4+ and CD8+ cells	Enthesitis skin inflammation synovitis	IL-6[7], IL-7[4], IL-15[4], IL-12[7], IL-23[2]	IL-17[4], IL-22[4]
Dendritic cells	T cell activation	IL-15[4], IFNα[3]	IFNγ[4], IL-12[2], IL-23[2]
Innate lymphoid cells	Enthesitis	IL-7[5]	IL-17[5], IL-22[5], TNF[5]
Keratinocytes	Hyperkeratosis systemic inflammation	IL-17[4], IL-22[1], IL-20 family[1]	
Lymphocyte synoviocyte interaction	Synovial inflammation	IL-15[8], IFNγ[8], IL-17[8]	RANKL[6], TNF[3]
Osteoclast	Bone resorption	RANKL[6], IL-6[6], TNF[3]	
Osteoblast	Pathologic bone formation	IL-22[3]	

CD=Cluster of Differentiation; IFN=Interferon; RANKL=Receptor Activator of Nuclear factor Kappa-B Ligand

1. O'Sullivan, LA et al. *Mol Immunol* 2007, *44* (10), 2497-506.; 2. McInnes, IB et al. *N Engl J Med* 2011, *365* (23), 2205-19.; 3. Ritchlin, CT et al. *N Engl J Med* 2017, *376* (10), 957-970.; 4. Krueger, J et al. *J Allergy Clin Immunol* 2016, *137* (4), 1079-90.; 5. Shikhagaie, MM et al. *Nat Rev Rheumatol* 2017, *13* (3), 164-173.; 6. LaBranche, TP et al. *Arthritis Rheum* 2012, *64* (11), 3531-42.; 7. Ghoreschi, K et al. *J Immunol* 2011, *186* (7), 4234-43.; 8. Miranda-Carus, ME et al. *J Immunol* 2004, *173* (2), 1463-76.

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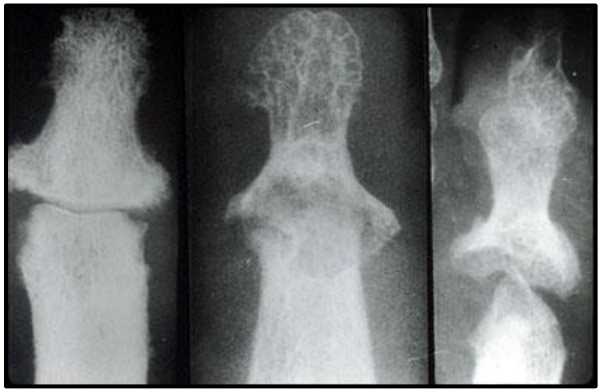

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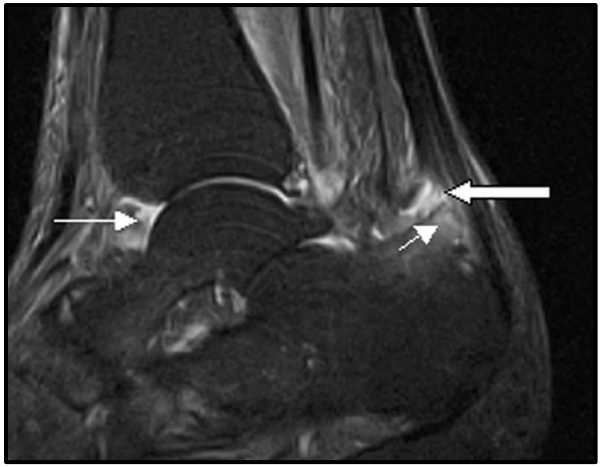

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Cytokines in red are JAK dependent

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Pathogenic Pathways

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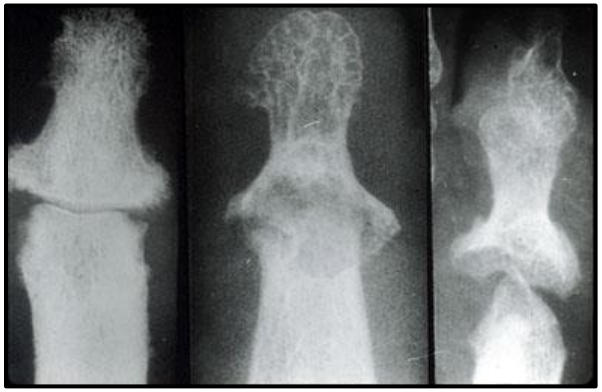

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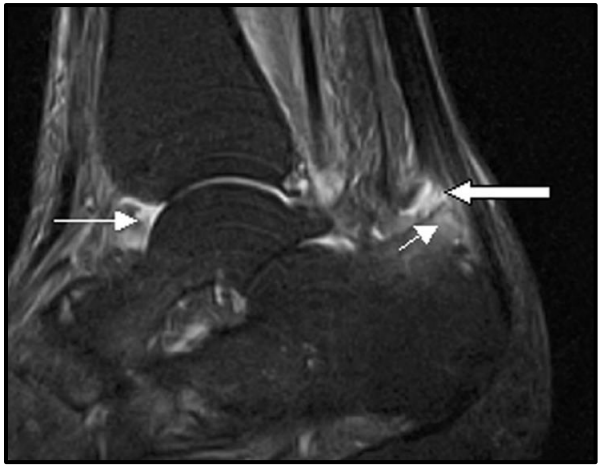

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Cytokines in red are JAK dependent
Tofacitinib reduces the production or downstream effects of cytokines in blue

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Summary

- Psoriatic arthritis has numerous clinical manifestations
  - Resulting in physical disability and psychosocial impact
- Each patient with PsA is clinically unique
  - The disease burden is typically high
- Despite the availability of several therapeutic options
  - Drugs to treat patients with active PsA all have limitations
- A need exists for medications that work across the spectrum of cytokines involved in the pathogenesis of PsA with a convenient mode of delivery, i.e. oral
  - Tofacitinib has a well-characterized efficacy and safety profile well known to rheumatologists who have used it in RA

Overview of Presentation

Topic	Presenter
Introduction	Nancy McKay Director, Regulatory Affairs Pfizer Inc
Psoriatic Arthritis: A Rheumatologist's Perspective/ Unmet Medical Need	Philip Mease, MD, MACR Director, Rheumatology Research, Swedish-Providence-St. Joseph's Health Systems Clinical Professor, University of Washington School of Medicine, Seattle, WA
Tofacitinib PsA Development Program and Efficacy	**Keith Kanik, MD, FACR** **Senior Director, Global Clinical Lead PsA** **Inflammation and Immunology** **Pfizer Inc**
Tofacitinib PsA Safety	Daniela Graham, MD Clinician, PsA Development Program Inflammation and Immunology Pfizer Inc
Risk Management	Thomas Jones, MD Senior Director, Safety Risk Management Pfizer Inc
Benefit:Risk and Conclusions	Michael Corbo, PhD Senior VP, Chief Development Officer Inflammation and Immunology Pfizer Inc

Tofacitinib PsA Development Program and Efficacy

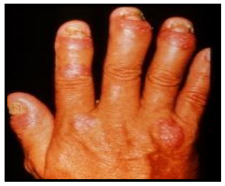
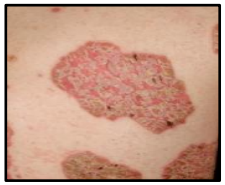
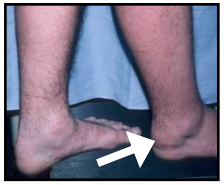
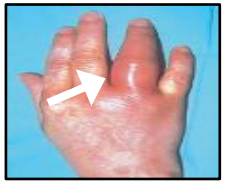
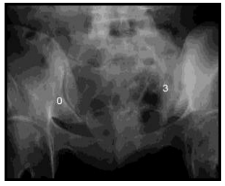
Keith Kanik, MD, FACR

Senior Director, Global Clinical Lead PsA

Inflammation and Immunology

Pfizer Inc

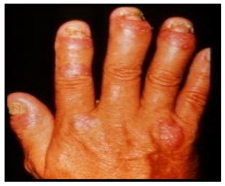
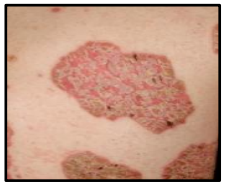
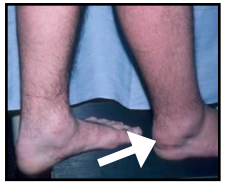
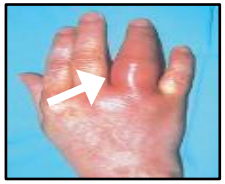
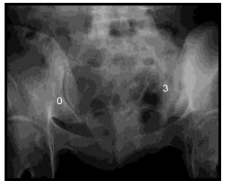
Psoriatic Arthritis is a Complex Disease

Study Endpoints Associated with PsA Disease Manifestations		
Peripheral Arthritis		▪ ACR 20/50/70 response rates ▪ Health Assessment Questionnaire-Disability Index (HAQ-DI) ▪ Radiographic evaluation of structural damage
Psoriasis		▪ Psoriasis Area and Severity Index (PASI) ▪ Physician's Global Assessment of Psoriasis (PGA-PsO)
Enthesitis		▪ Leeds Enthesitis Index (LEI); Enthesitis resolution (LEI) ▪ SPARCC Enthesitis Index score; Enthesitis resolution (SPARCC)
Dactylitis		▪ Dactylitis Severity Score (DSS) ▪ Dactylitis absence
Spondylitis		▪ Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)

SPARCC=Spondyloarthritis Research Consortium of Canada

Psoriatic Arthritis is a Complex Disease

Study Endpoints Associated with PsA Disease Manifestations

Peripheral Arthritis		▪ **ACR 20/50/70 response rates** ▪ **Health Assessment Questionnaire-Disability Index (HAQ-DI)** ▪ **Radiographic evaluation of structural damage**
Psoriasis		▪ **Psoriasis Area and Severity Index (PASI)** ▪ **Physician's Global Assessment of Psoriasis (PGA-PsO)**
Enthesitis		▪ **Leeds Enthesitis Index (LEI)**; **Enthesitis resolution (LEI)** ▪ **SPARCC Enthesitis Index score; Enthesitis resolution (SPARCC)**
Dactylitis		▪ **Dactylitis Severity Score (DSS)** ▪ **Dactylitis absence**
Spondylitis		▪ **Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)**

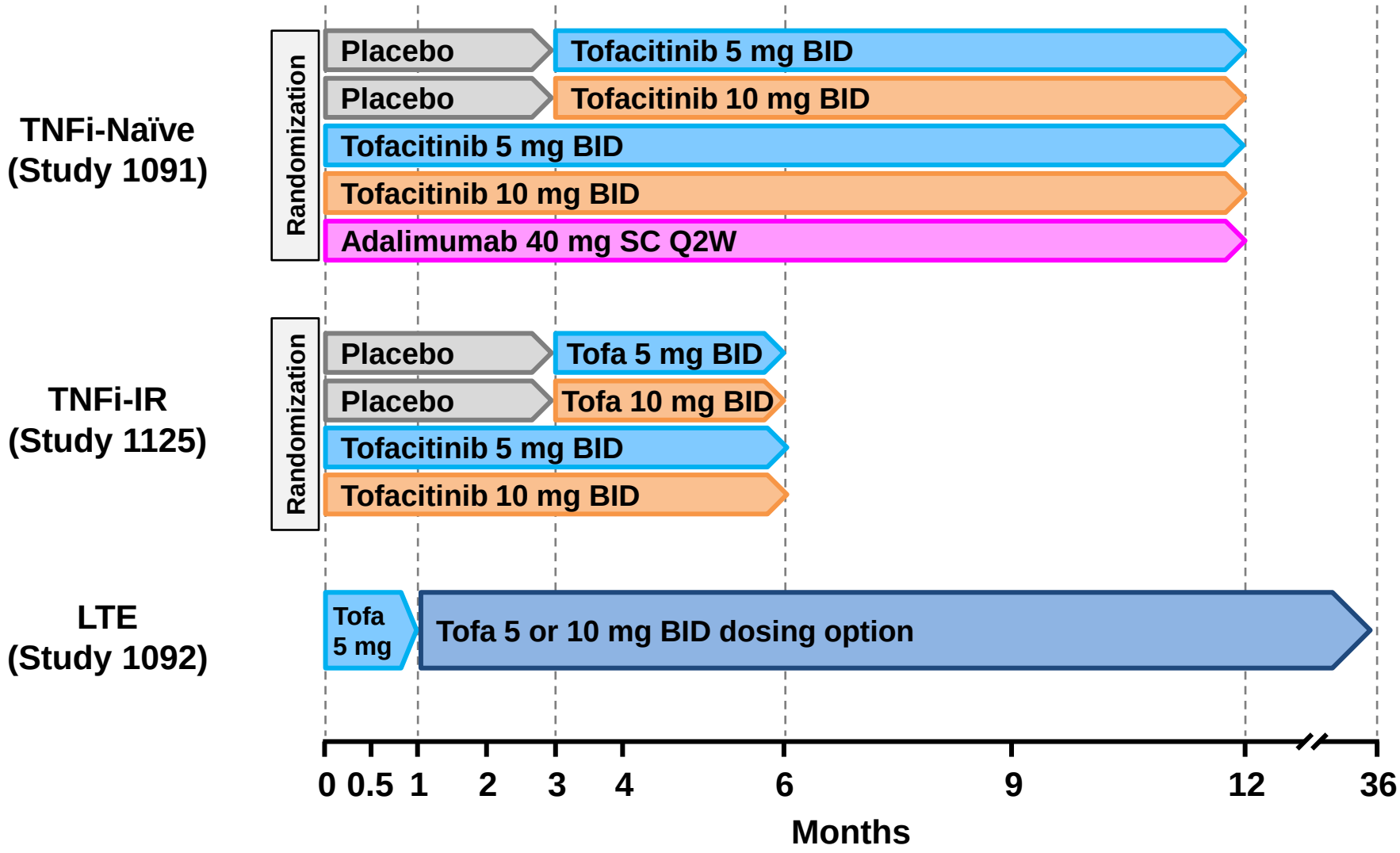
SPARCC=Spondyloarthritis Research Consortium of Canada

CASPAR Criteria to Classify PsA

- To meet the CASPAR (Classification Criteria for Psoriatic Arthritis) criteria, a patient must have inflammatory articular disease (joint, spine, or entheseal) with 3 points from the following 5 categories

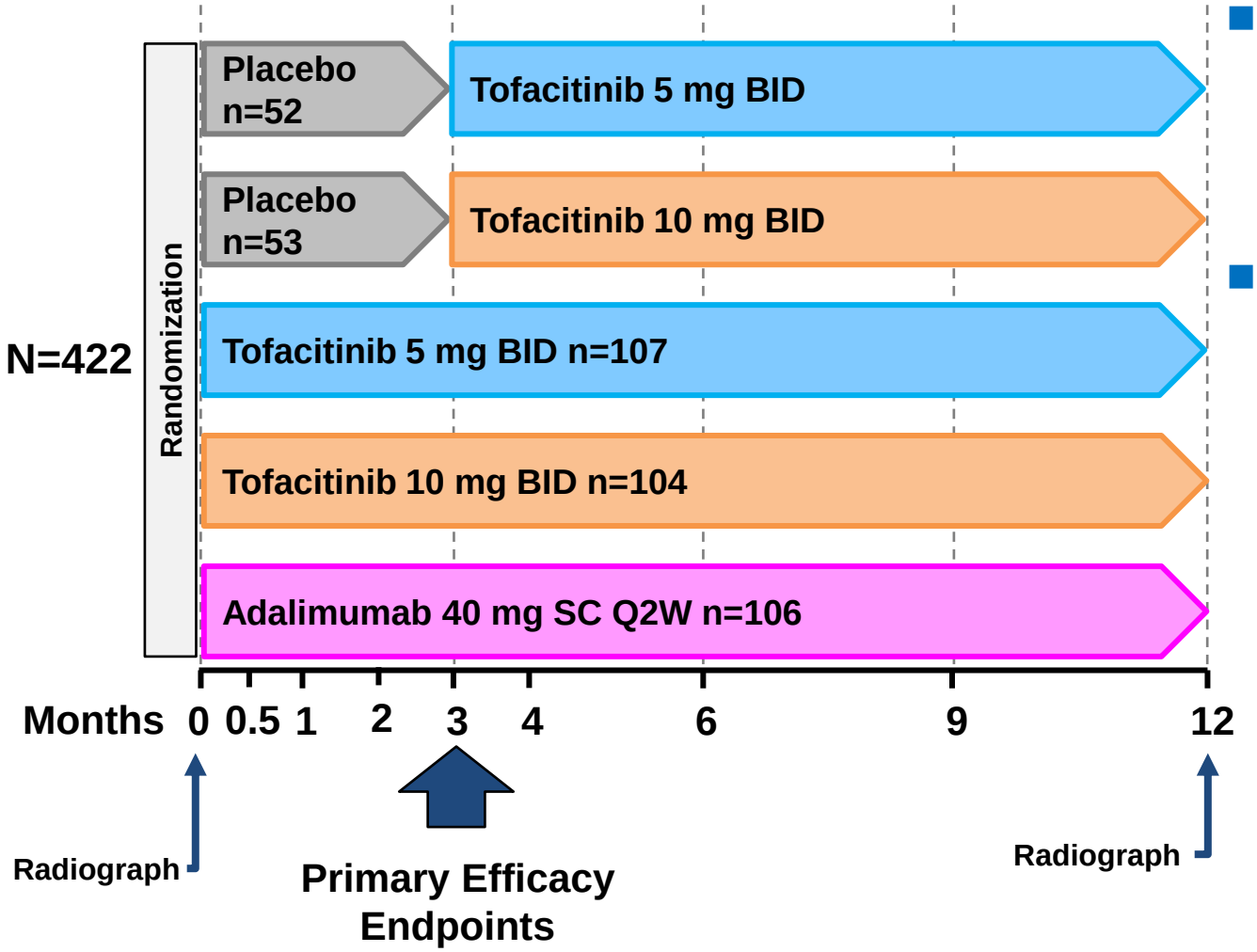
  1. Evidence of current psoriasis, a personal history of psoriasis, or a family history of psoriasis
  2. Typical psoriatic nail dystrophy including oncholysis, pitting, and hyperkeratosis observed on current physical examination
  3. A negative test result for the presence of rheumatoid factor by any method except latex but preferably by enzyme-linked immunosorbent assay or nephelometry, according to the local laboratory reference range
  4. Either current dactylitis or a history of dactylitis recorded by a rheumatologist
  5. Radiographic evidence of juxta-articular new bone formation, appearing as ill-defined ossification near joint margins (but excluding osteophyte formation) on plain radiographs of the hand or foot

Tofacitinib PsA Phase 3 Program Design



LTE=Long-Term Extension; Q2W=once every two weeks; SC=Subcutaneously

TNFi-Naïve Patient Study Design (Study 1091)

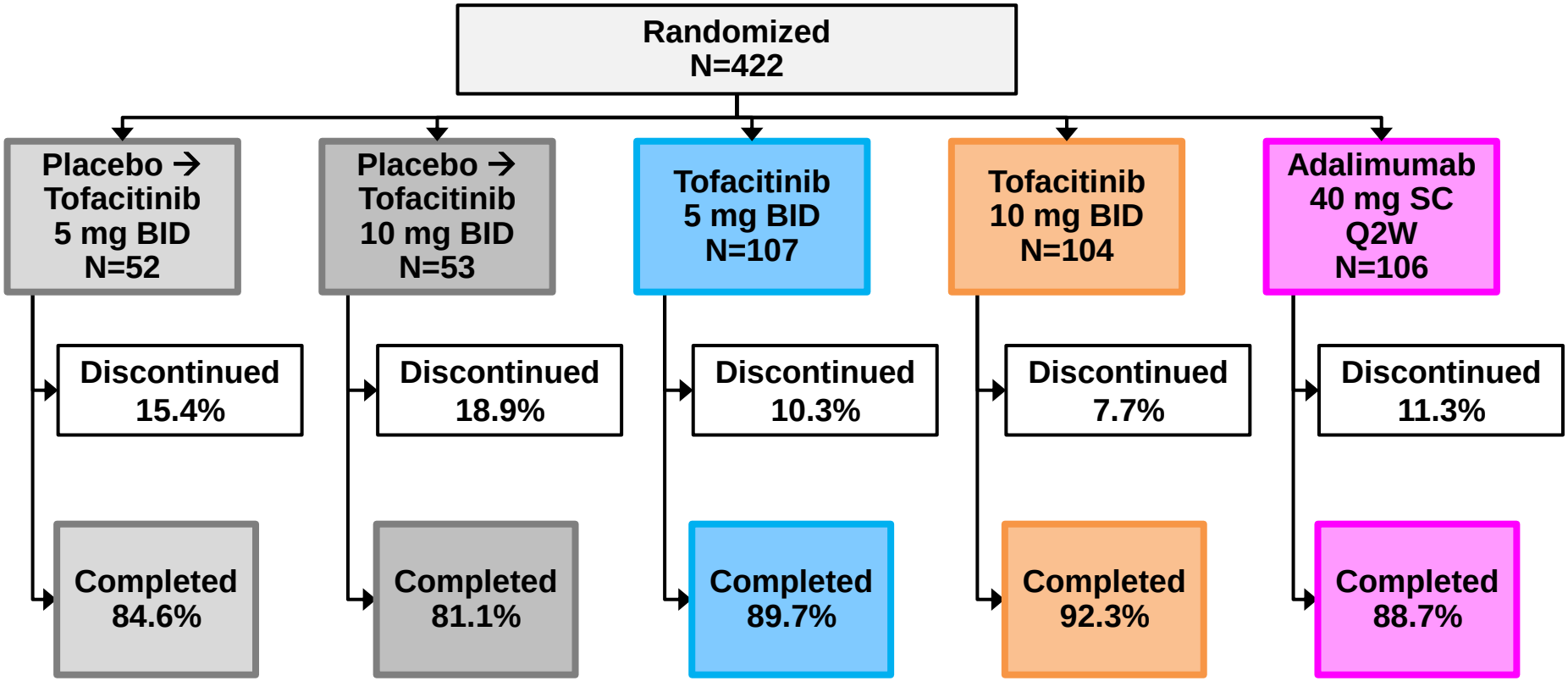


- **Primary Efficacy Endpoints (Month 3)**
  - **ACR20**
  - **ΔHAQ-DI**
- Secondary Efficacy Endpoints (Month 3)
  - PASI75
  - ΔLEI
  - ΔDSS
  - ΔSF-36v2 PF
  - ΔFACIT-F

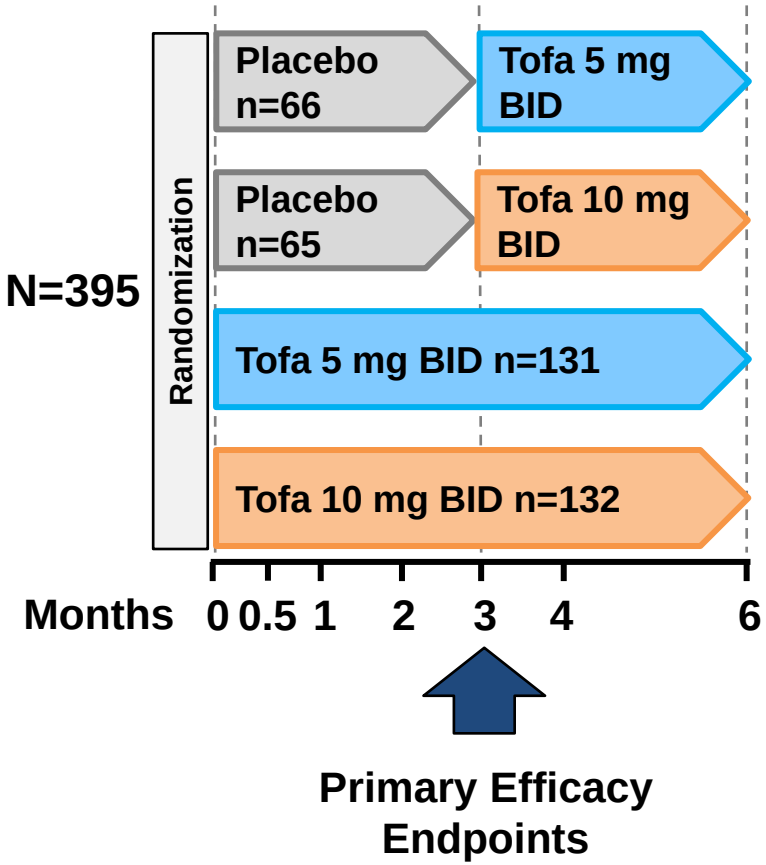
  - ACR50, ACR70: Month 3
  - ACR20: pre-Month 3

FACIT-F=Functional Assessment of Chronic Illness Therapy-Fatigue; PASI75=75% improvement in the Psoriasis Area and Severity Index; SF-36v2 PF=Short Form-36 version 2, Physical Functioning subscale

Patient Disposition in TNFi-Naïve Study (Study 1091)



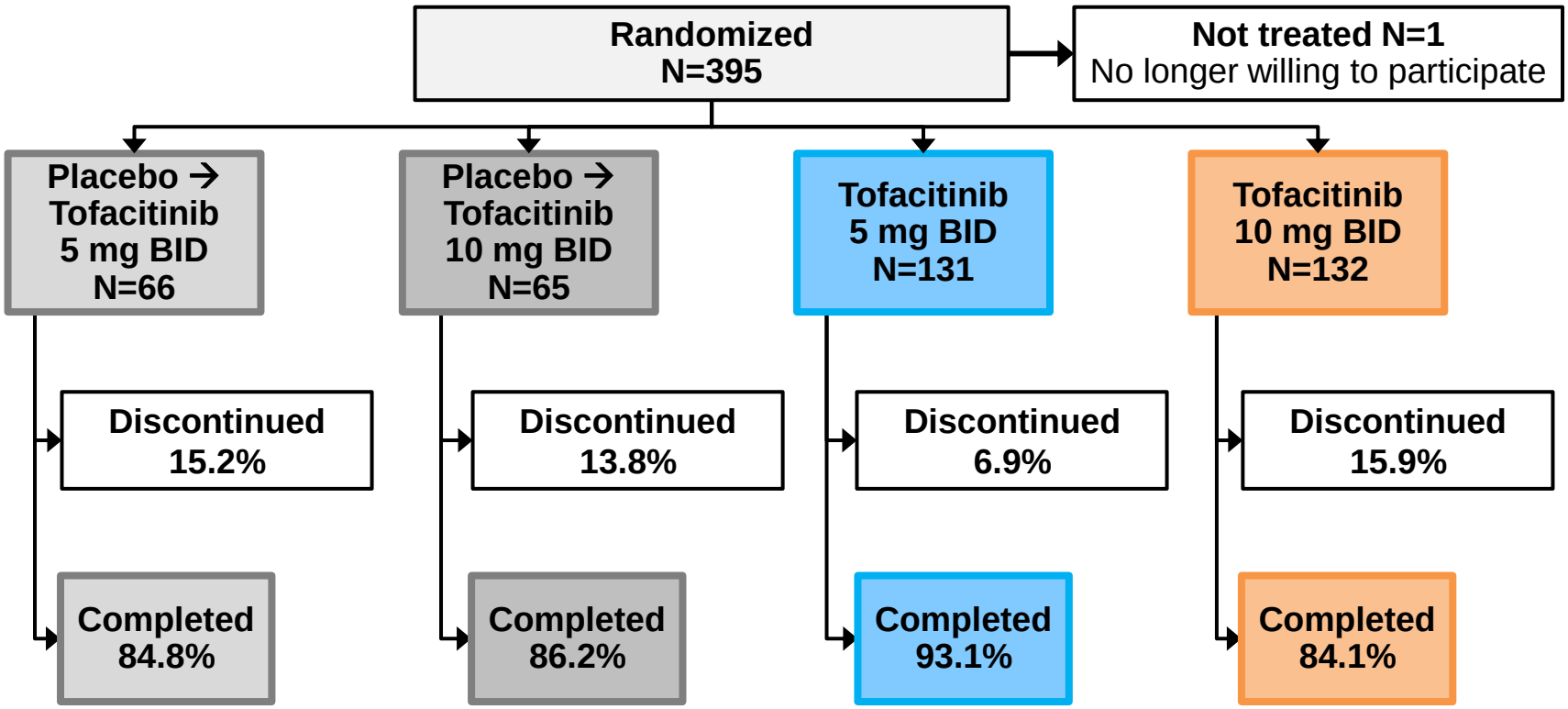
TNFi-Inadequate Responder (TNFi-IR) Study Design (Study 1125)



- **Primary Efficacy Endpoints (Month 3)**
  - **ACR20**
  - **ΔHAQ-DI**
- Secondary Efficacy Endpoints (Month 3)
  - PASI75
  - ΔLEI
  - ΔDSS
  - ΔSF-36v2 PF
  - ΔFACIT-F

  - ACR50, ACR70: Month 3
  - ACR20: pre-Month 3

Patient Disposition in TNFi-IR Study (Study 1125)

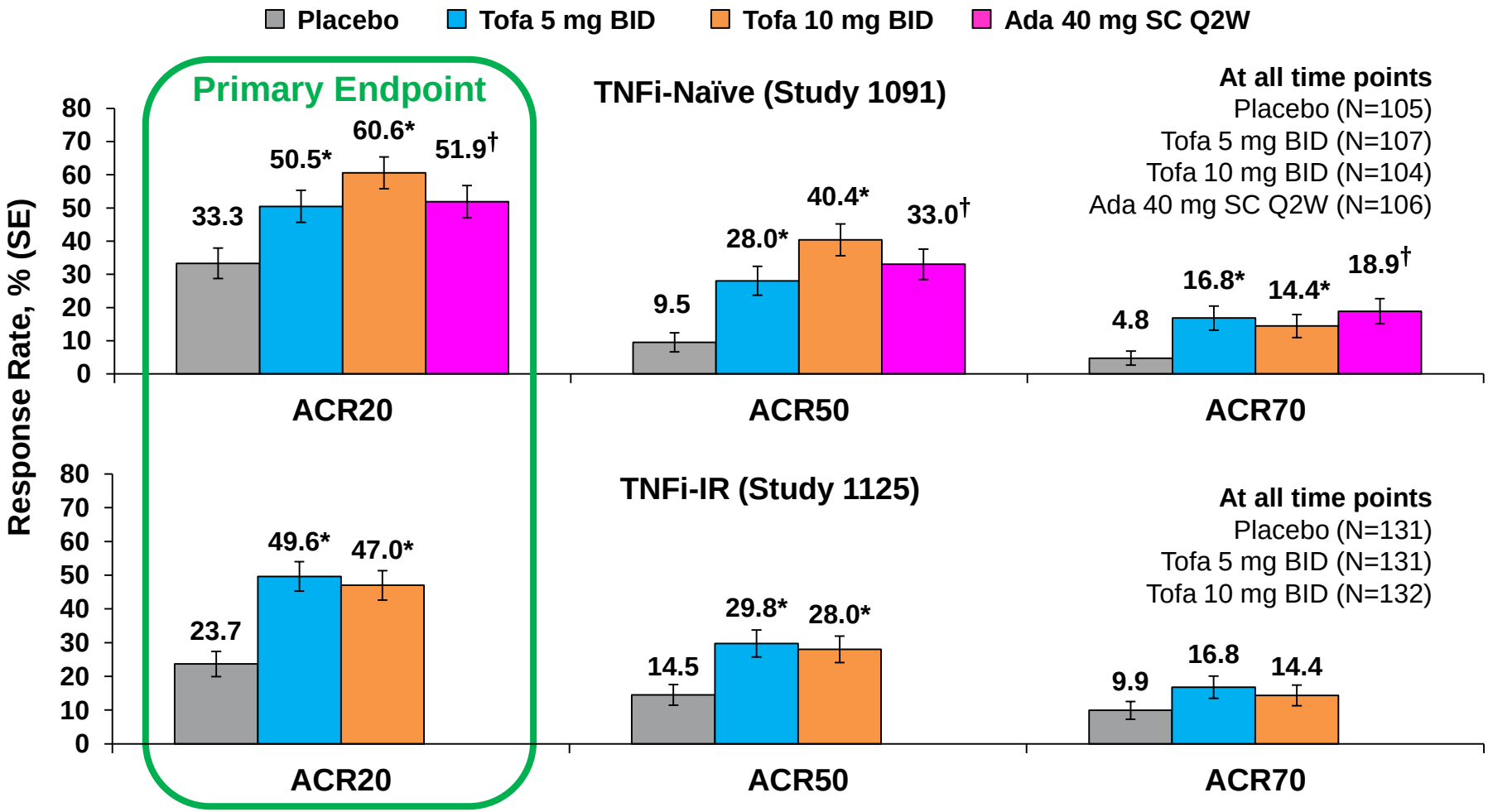


Similar Baseline Demographics and Disease Characteristics Between PsA Studies

	TNFi-Naïve (Study 1091) N=422	TNFi-IR (Study 1125) N=394
Male, n (%)	197 (46.7)	176 (44.7)
Age, mean, years (SD)	47.9 (12.1)	50.0 (12.0)
White, n (%)	409 (96.9)	363 (92.1)
Mean PsA duration, years	6.1	9.4
Patients with BSA≥3% psoriasis, %	73.9	62.7
Patients with enthesitis, LEI >0, %	66.4	69.8
Patients with dactylitis, DSS >0, %	56.2	49.2
Mean swollen joint count	11.5	11.8
Mean tender joint count	19.6	22.0
Median CRP, mg/L (ULN 2.87 mg/L)	4.89	4.73
Mean HAQ-DI	1.11	1.30
Patients with concomitant csDMARD use, %	100.0	99.0
MTX use, %	83.9	71.6
Patients with oral corticosteroid use, %	19.2	24.1

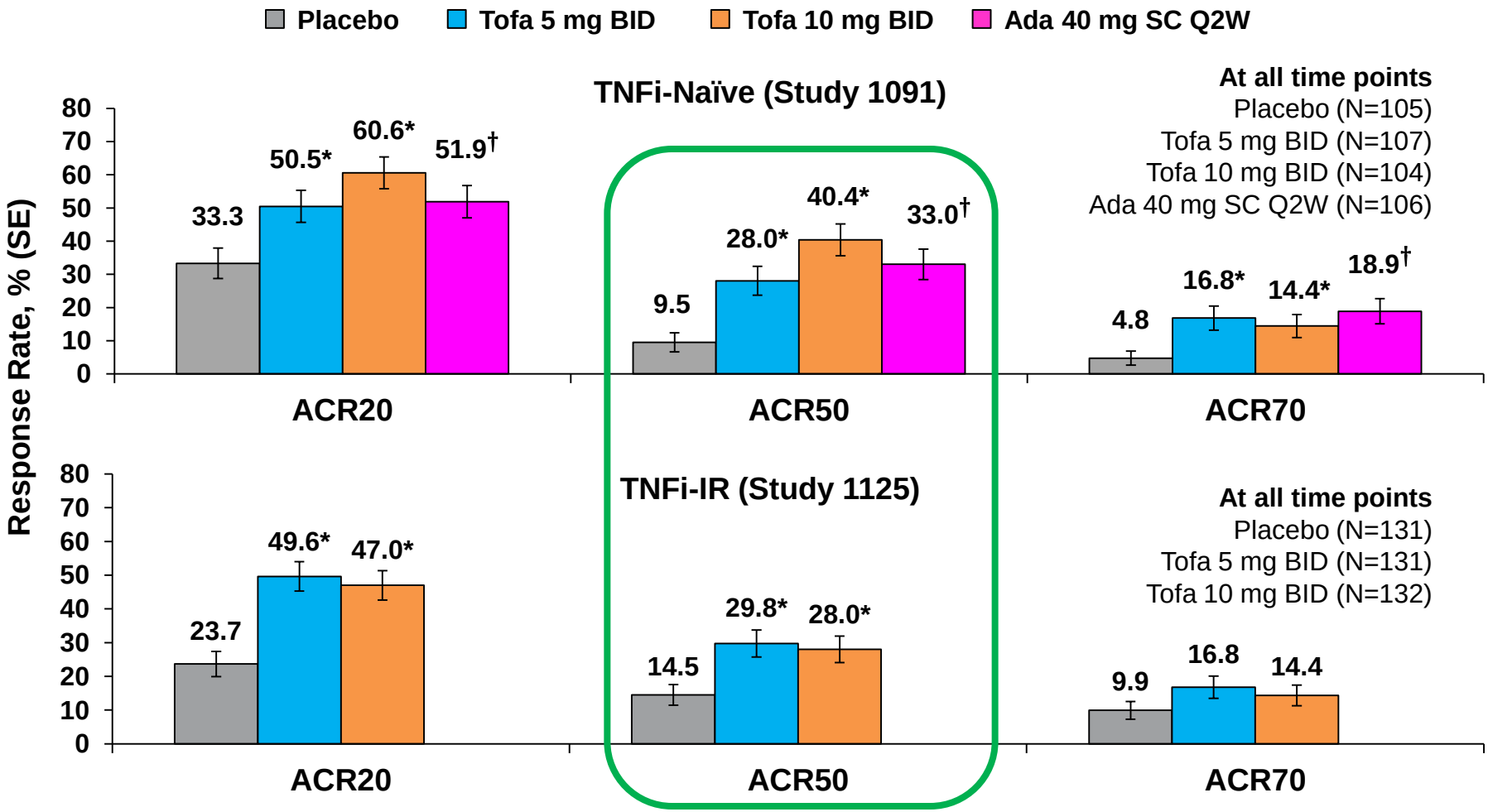
BSA=Body Surface Area; CRP=C-Reactive Protein; csDMARD=conventional synthetic Disease Modifying Anti-Rheumatic Drugs; SD=Standard Deviation; ULN=Upper Limit of Normal

Significant Improvement in Peripheral Arthritis (Month 3)



*Achieved statistical significance under Type I error control
†95% CI for difference between active treatment and placebo excluded zero
FAS, MR=NR
CI=Confidence Interval; SE=Standard Error

Significant Improvement in Peripheral Arthritis (Month 3)



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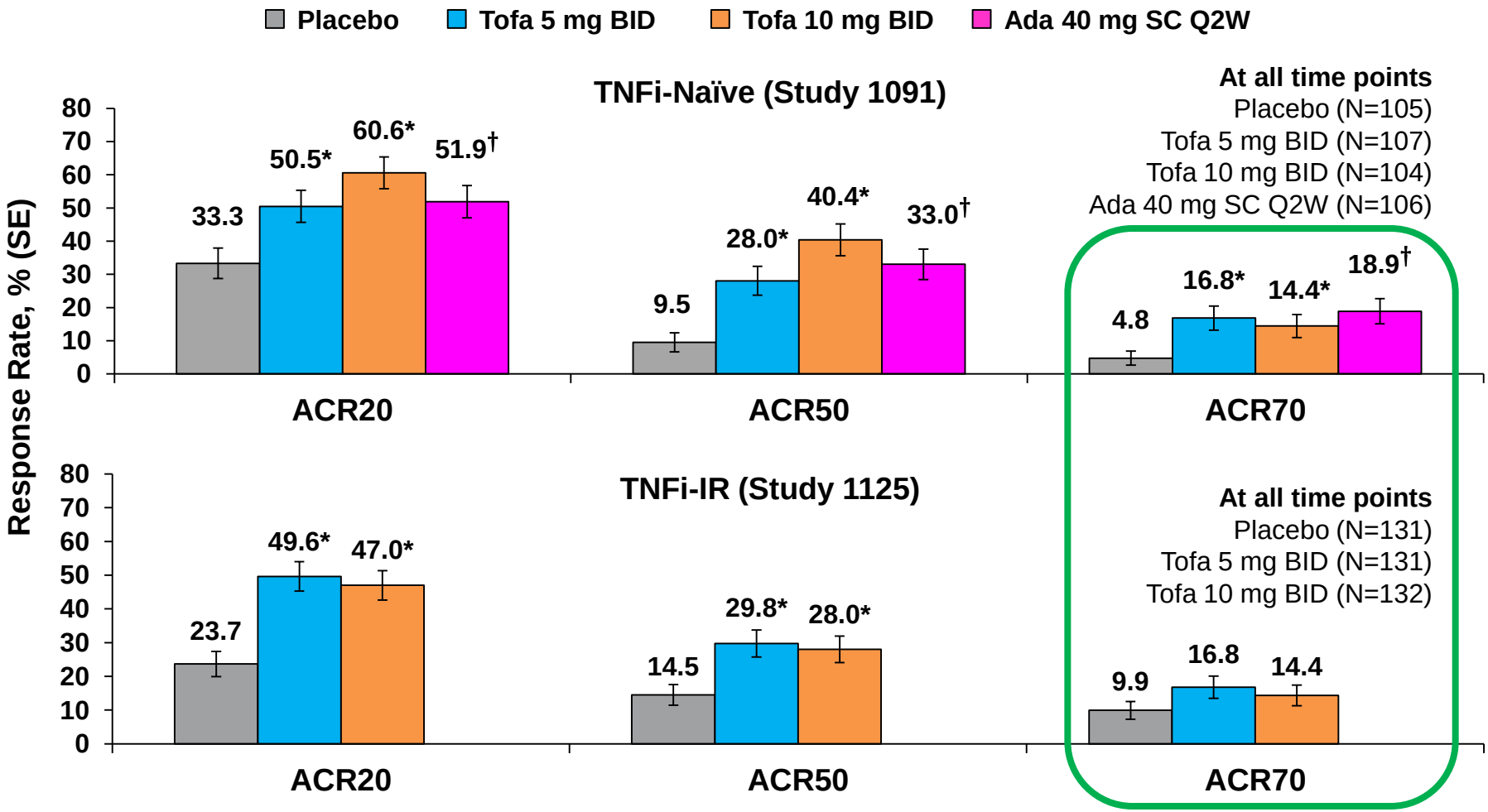
Significant Improvement in Peripheral Arthritis (Month 3)



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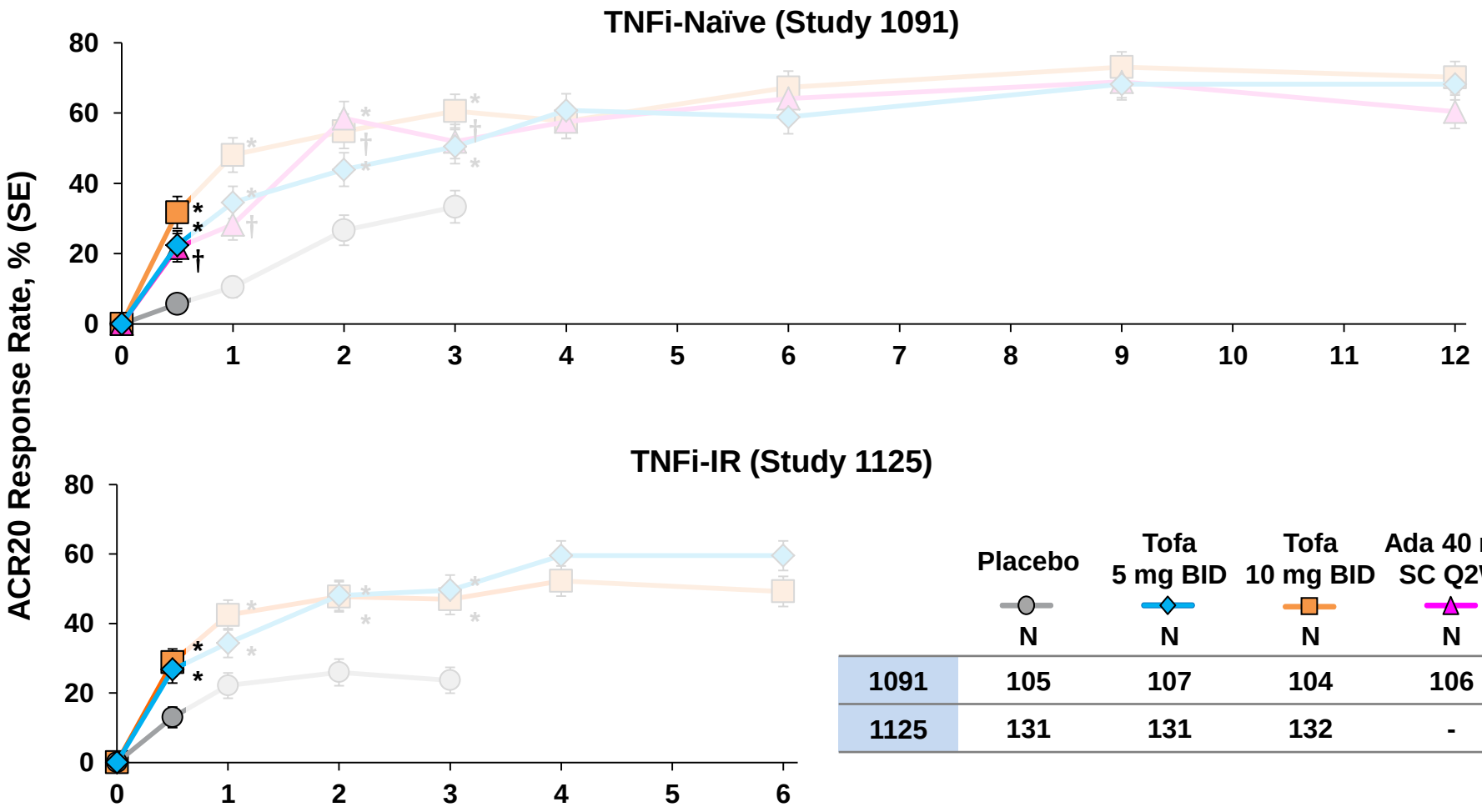
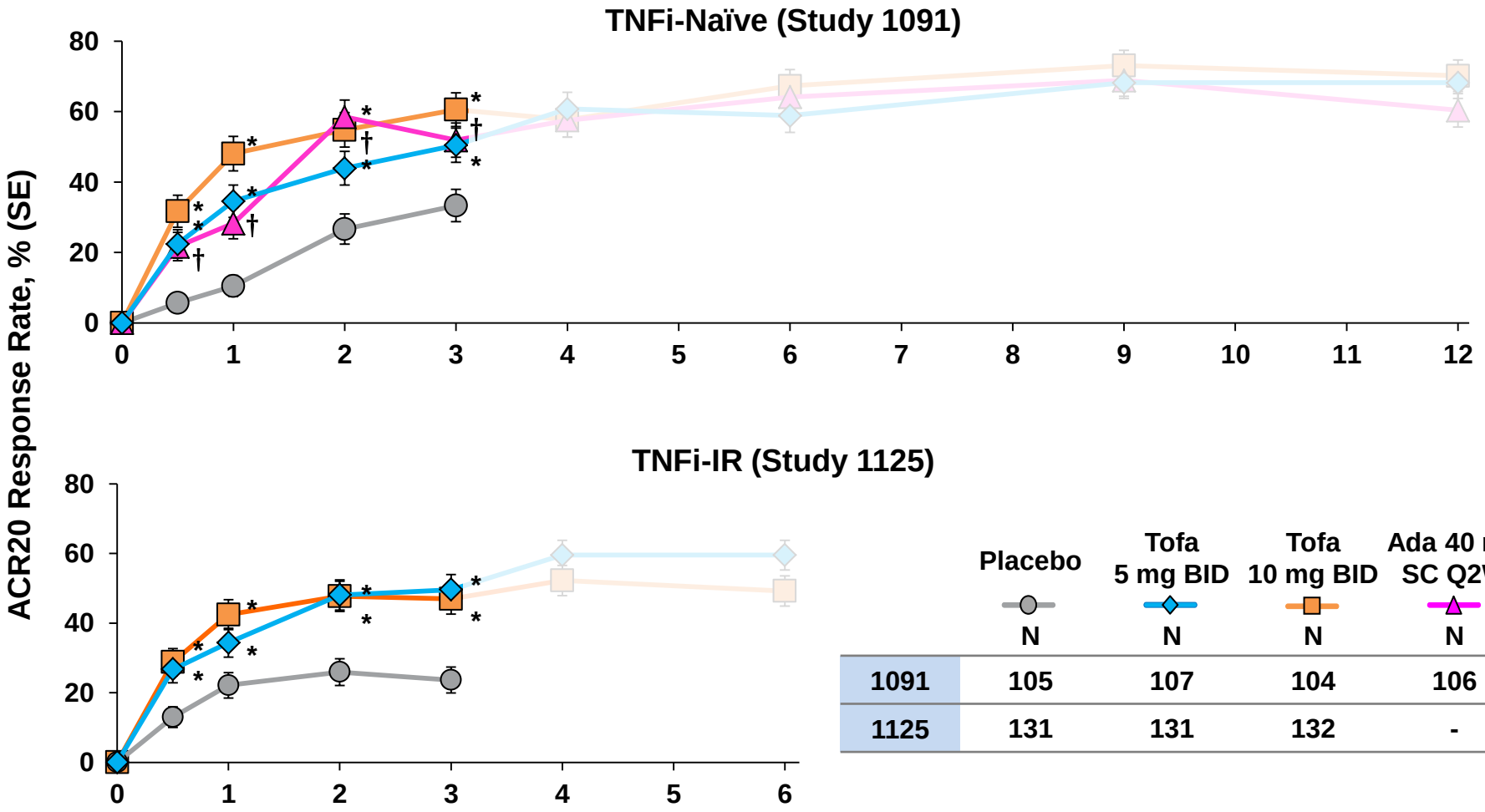
Onset of Efficacy at 2 Weeks



	Placebo N	Tofa 5 mg BID N	Tofa 10 mg BID N	Ada 40 mg SC Q2W N
1091	105	107	104	106
1125	131	131	132	-

*Achieved statistical significance under Type I error control
†95% CI for difference between active treatment and placebo excluded zero
FAS, MR=NR
FAS=Full Analysis Set; MR=NR=Missing Response=Non-Response; N=Number of patients in FAS

Efficacy First Observed at 2 Weeks Continued to Improve to Month 3



*Achieved statistical significance under Type I error control
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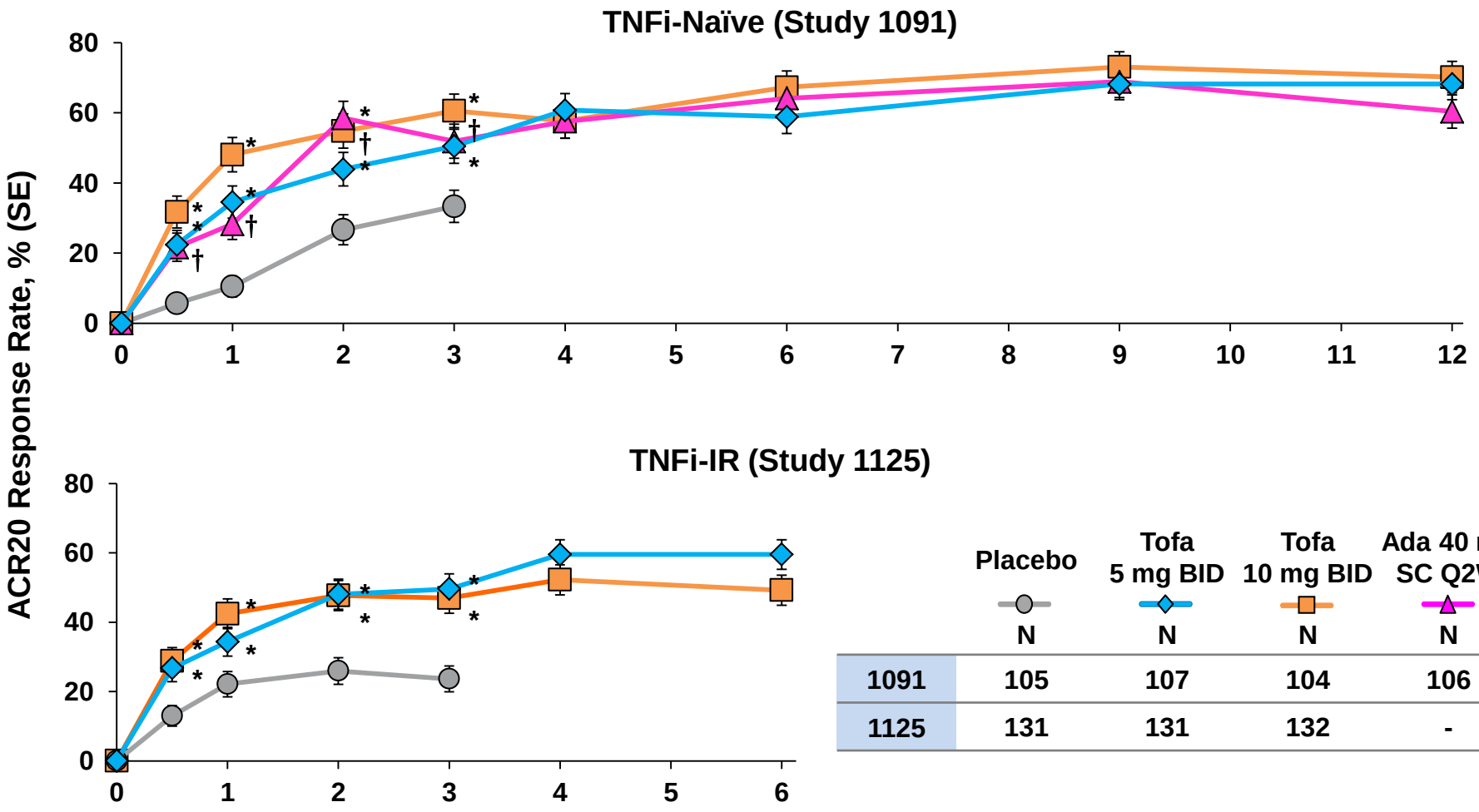
FAS, MR=NR
FAS=Full Analysis Set; MR=NR=Missing Response=Non-Response; N=Number of patients in FAS

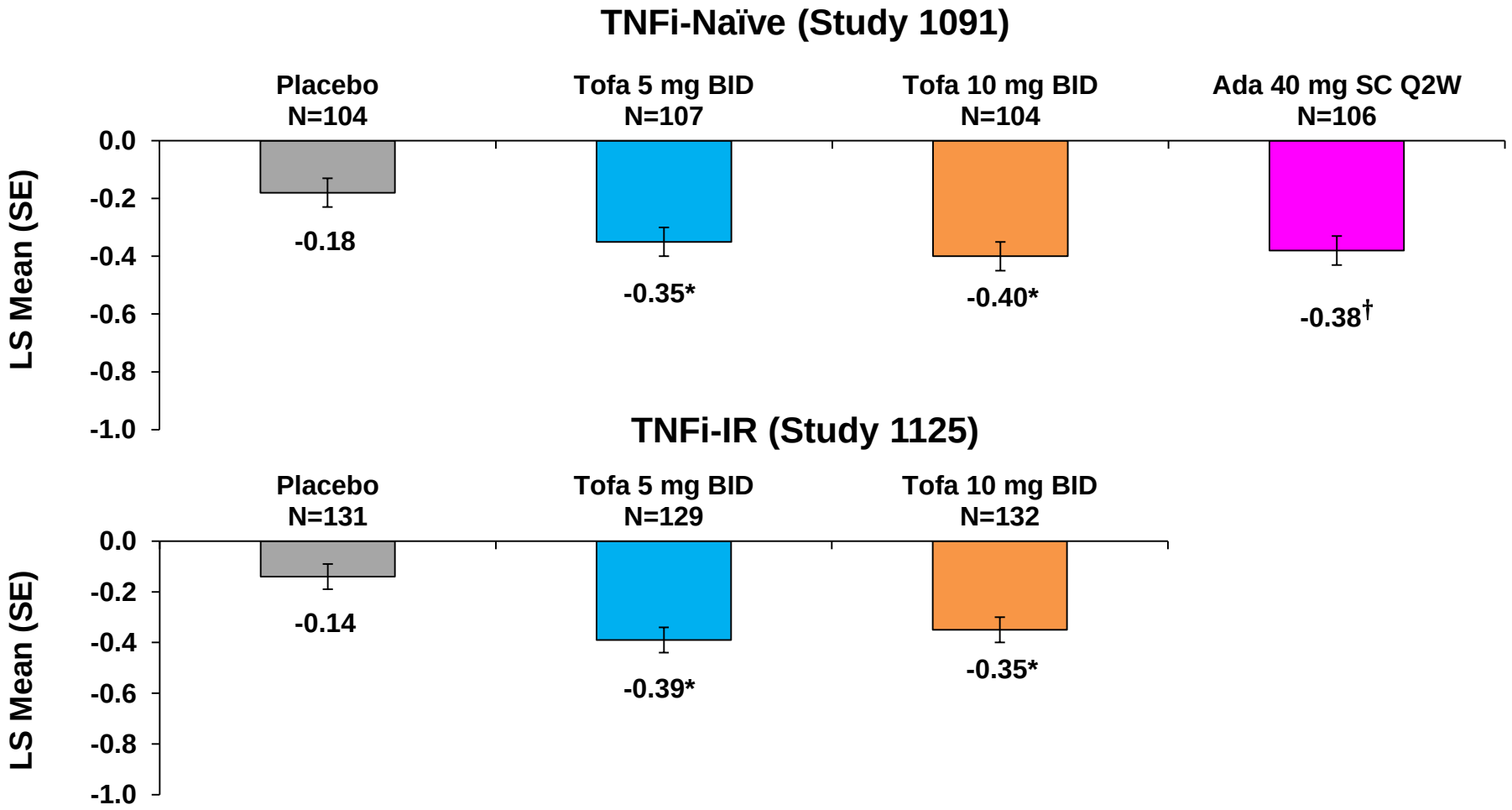
Efficacy Improved or Maintained Beyond Month 3



	Placebo N	Tofa 5 mg BID N	Tofa 10 mg BID N	Ada 40 mg SC Q2W N
1091	105	107	104	106
1125	131	131	132	-

*Achieved statistical significance under Type I error control
†95% CI for difference between active treatment and placebo excluded zero
FAS, MR=NR
FAS=Full Analysis Set; MR=NR=Missing Response=Non-Response; N=Number of patients in FAS

Significant Improvements in ΔHAQ-DI (Month 3): Second Primary Endpoint

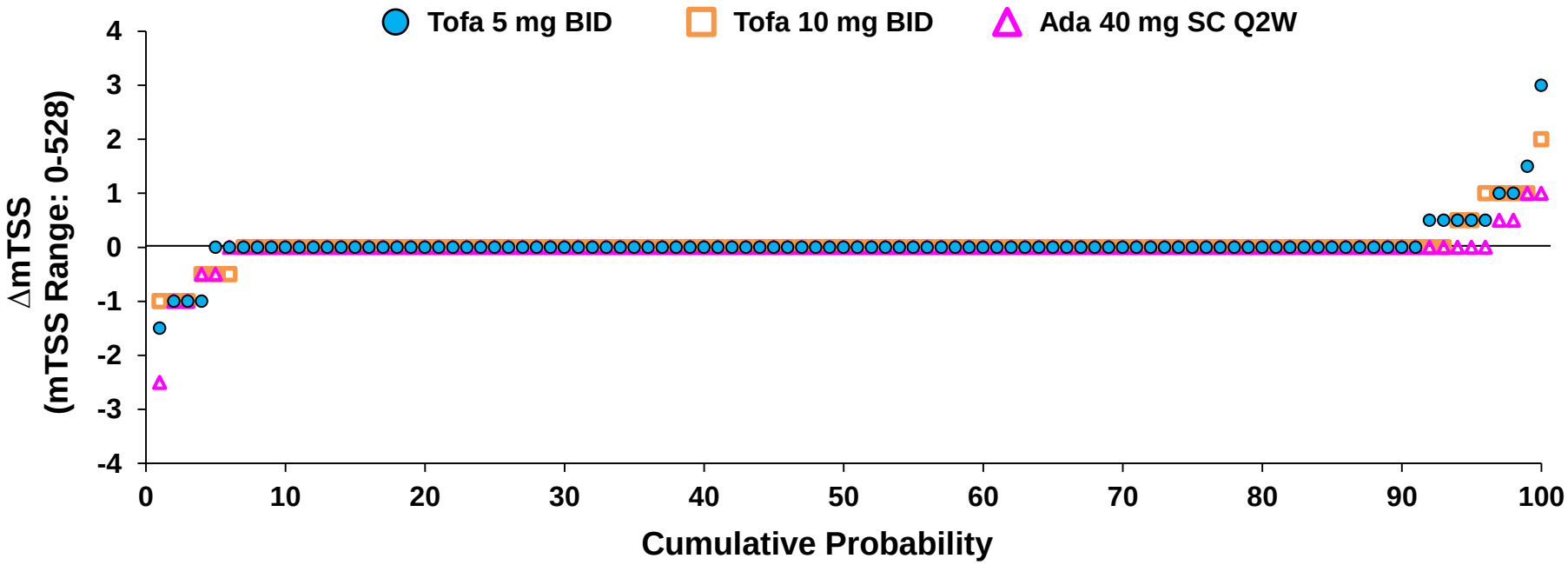


*Achieved statistical significance under Type I error control
†95% CI for difference between active treatment and placebo excluded zero
MMRM, FAS
LS=Least Square; MMRM=Mixed Model for Repeated Measures

Evaluation of Radiographic Progression

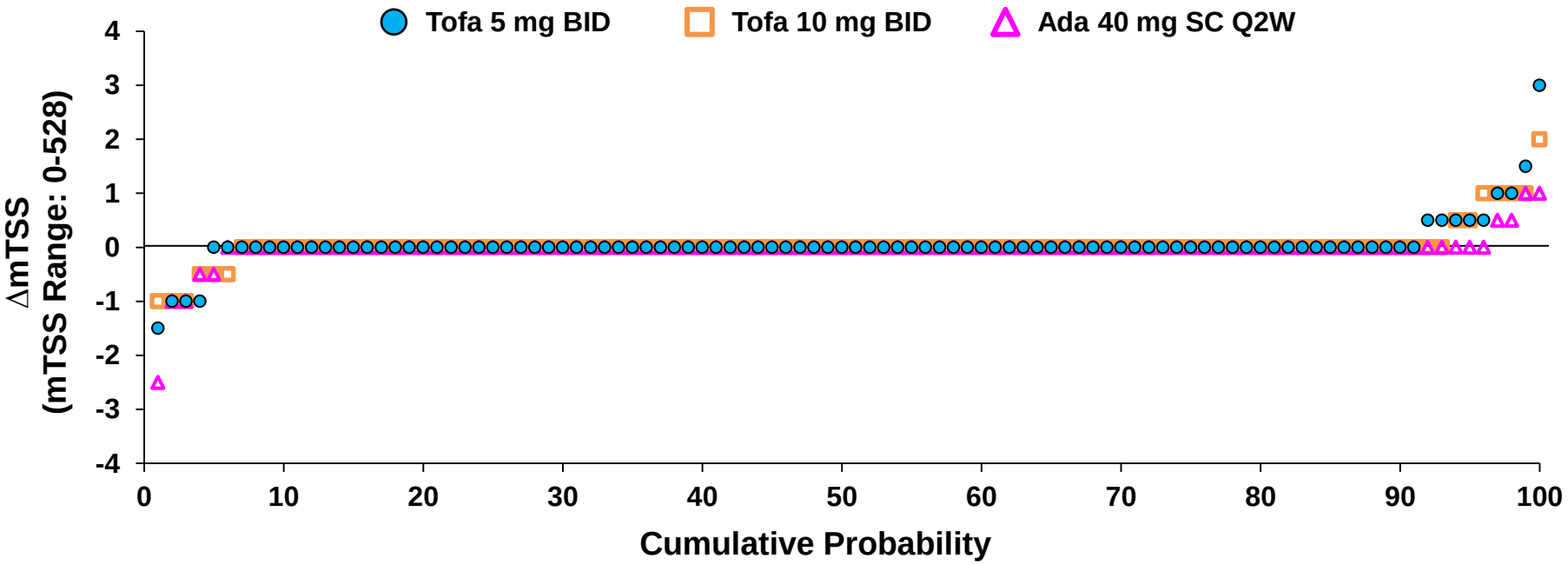
- Radiographs of hands and feet taken at baseline and Month 12 (or early termination) in TNFi-naïve patients (Study 1091)
- This pre-specified analysis was performed to assess lack of structural progression over 12 months of tofacitinib treatment
- Adalimumab 40 mg SC Q2W used as active comparator
- Study designed with consideration of regulatory agency advice

Change from Baseline in mTSS at Month 12 in TNFi-Naïve Patients (Study 1091)



FAS, Linear Extrapolation
mTSS=modified Total Sharp Score; N=number of subjects evaluable at Month 12 after linear extrapolation. n=number of progressors

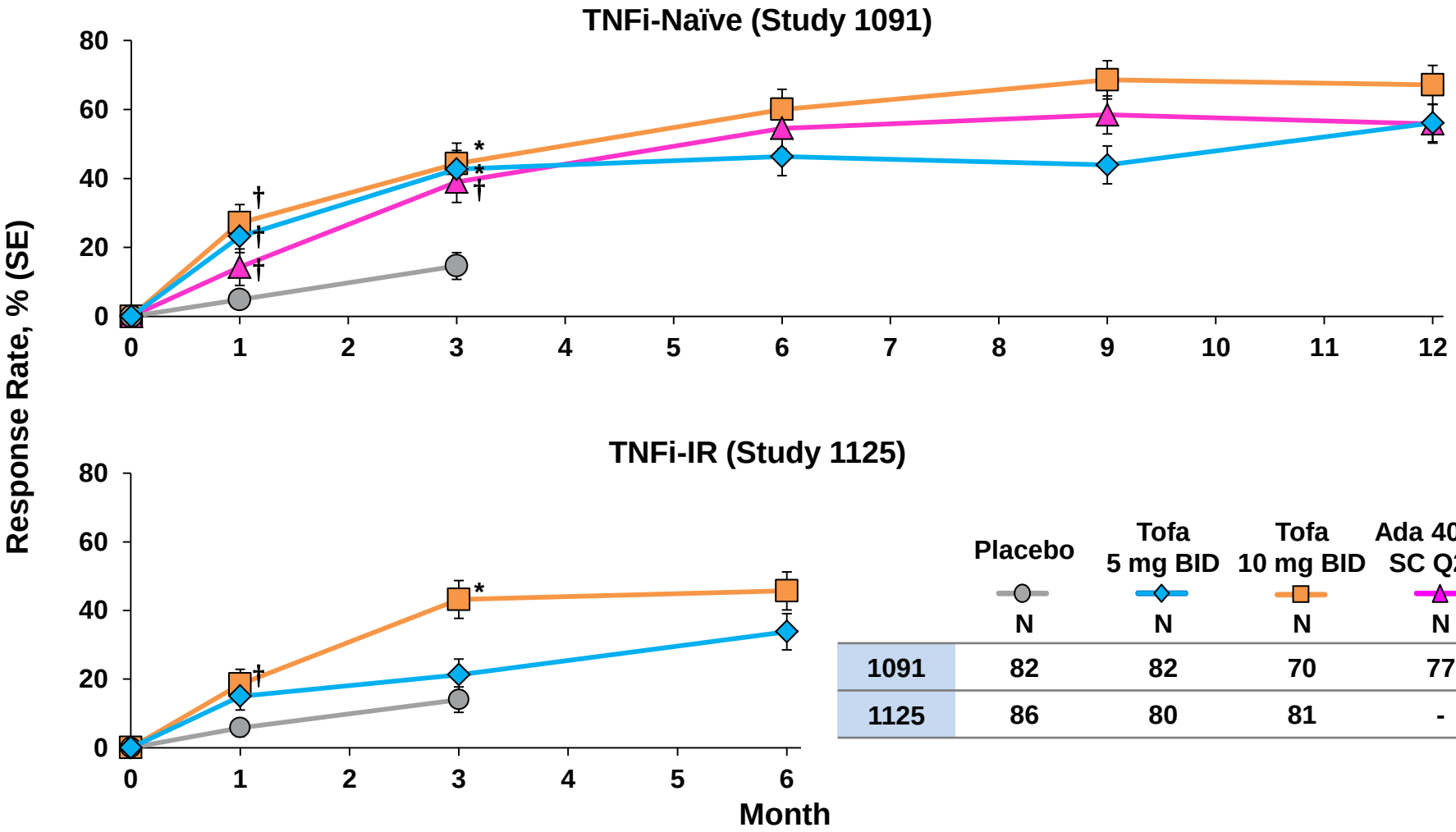
ΔmTSS and Progressor Rates at Month 12 in TNFi-Naïve Patients (Study 1091)



Progressor Rate at Month 12					
	N	ΔmTSS>0 n (%)	Difference from Ada 40 mg SC Q2W % (95% CI)	ΔmTSS>0.5 n (%)	Difference from Ada 40 mg SC Q2W % (95% CI)
Tofa 5 mg BID	98	9 (9.2)	5.0 (-2.0, 12.0)	4 (4.1)	2.0 (-2.9, 6.8)
Tofa 10 mg BID	99	7 (7.1)	2.9 (-3.6, 9.3)	5 (5.1)	3.0 (-2.3, 8.1)
Ada 40 mg SC Q2W	95	4 (4.2)	-	2 (2.1)	-

FAS, Linear Extrapolation
mTSS=modified Total Sharp Score; N=number of subjects evaluable at Month 12 after linear extrapolation. n=number of progressors

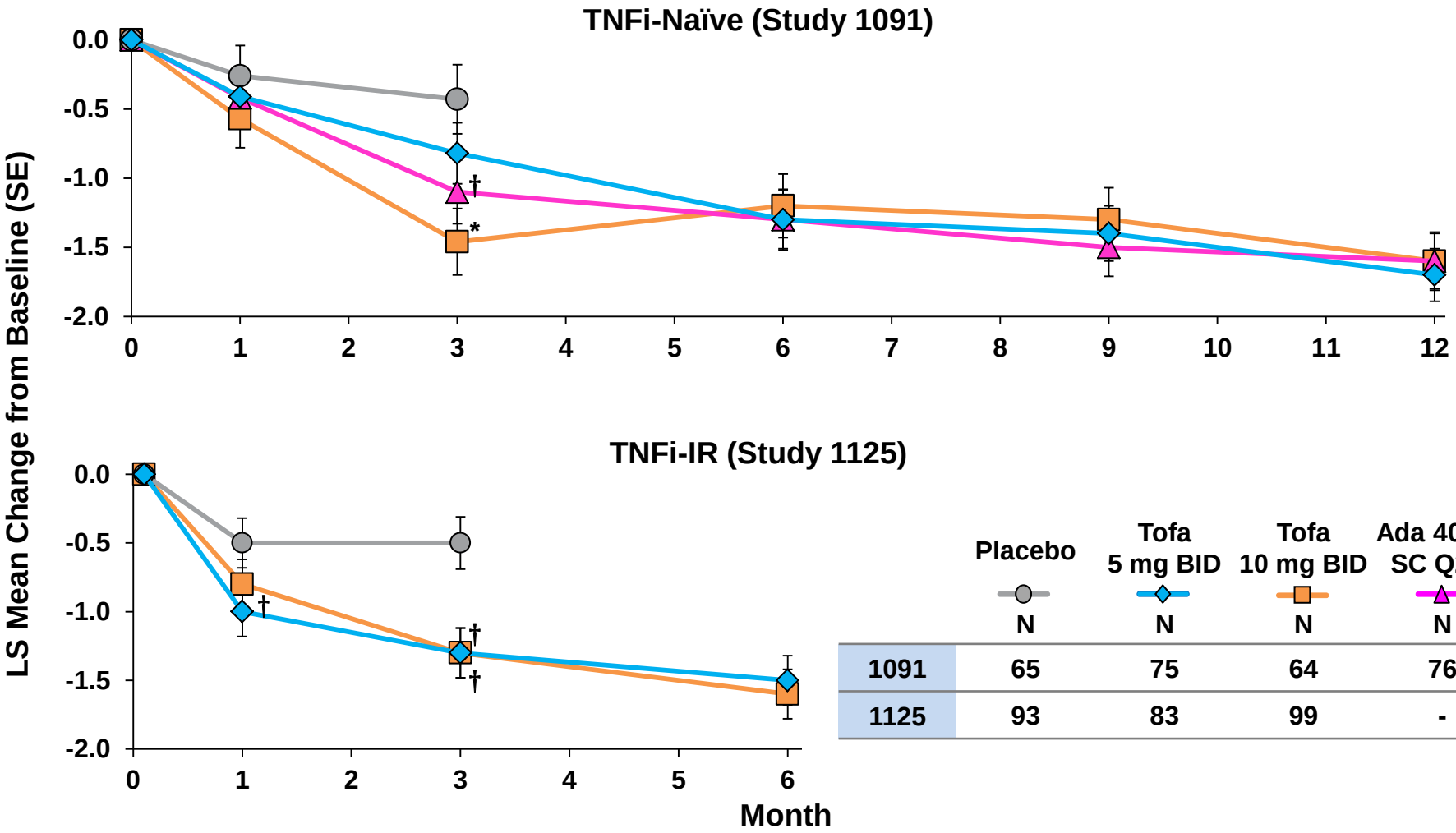
Improvements in Psoriasis (PASI75 Response Rate)



	Placebo	Tofa 5 mg BID	Tofa 10 mg BID	Ada 40 mg SC Q2W
	N	N	N	N
1091	82	82	70	77
1125	86	80	81	-

*Achieved statistical significance under Type I error control
†95% CI for difference between active treatment and placebo excluded zero
For patients with Baseline BSA≥3% and PASI>0 in FAS, MR=NR

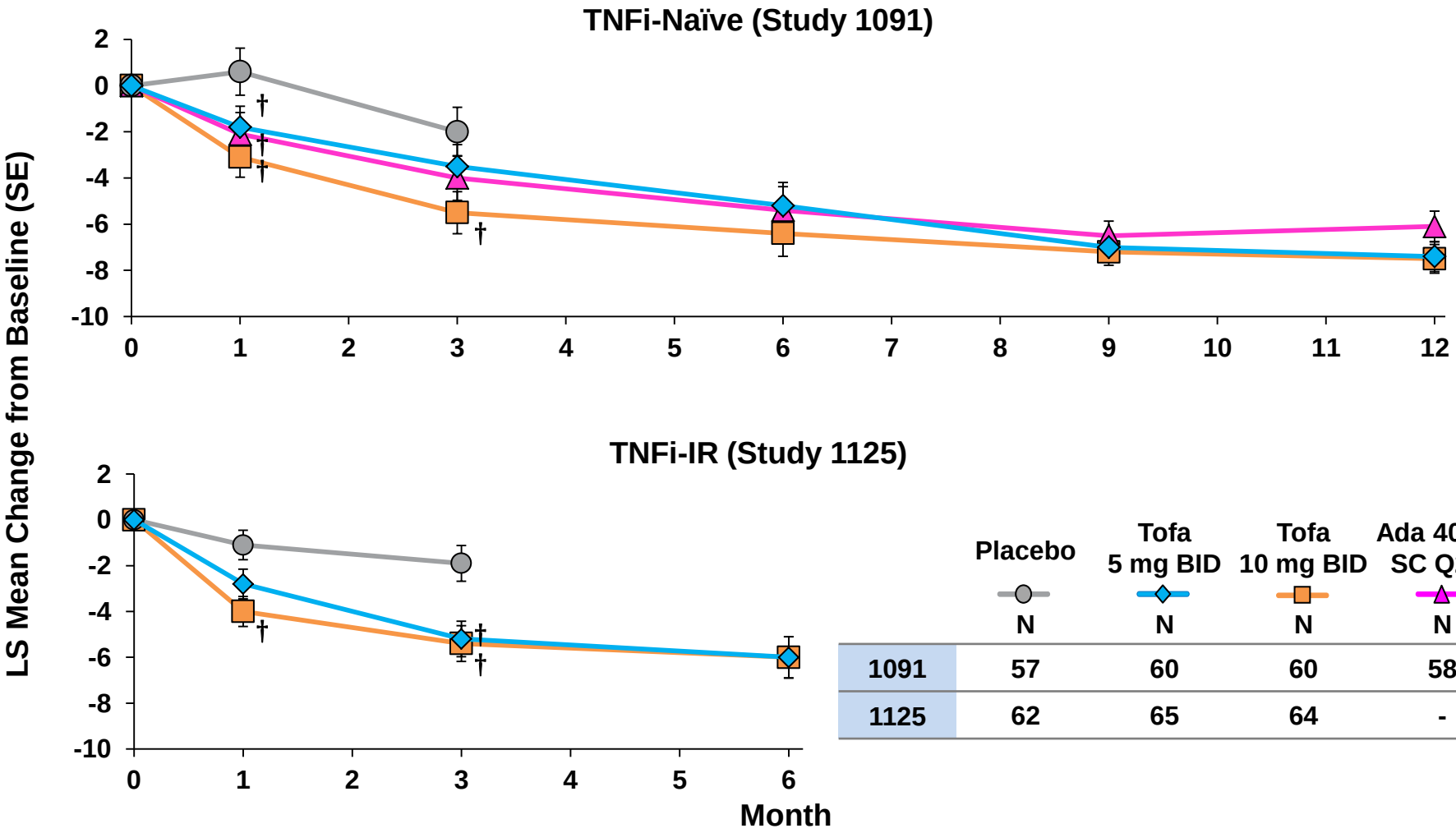
Improvements in Enthesitis (ΔLeeds Enthesitis Index)



	Placebo	Tofa 5 mg BID	Tofa 10 mg BID	Ada 40 mg SC Q2W
	N	N	N	N
1091	65	75	64	76
1125	93	83	99	-

*Achieved statistical significance under Type I error control
†95% CI for difference between active treatment and placebo excluded zero
For patients with Baseline LEI>0 in FAS, MMRM

Improvements in Dactylitis (ΔDactylitis Severity Score)

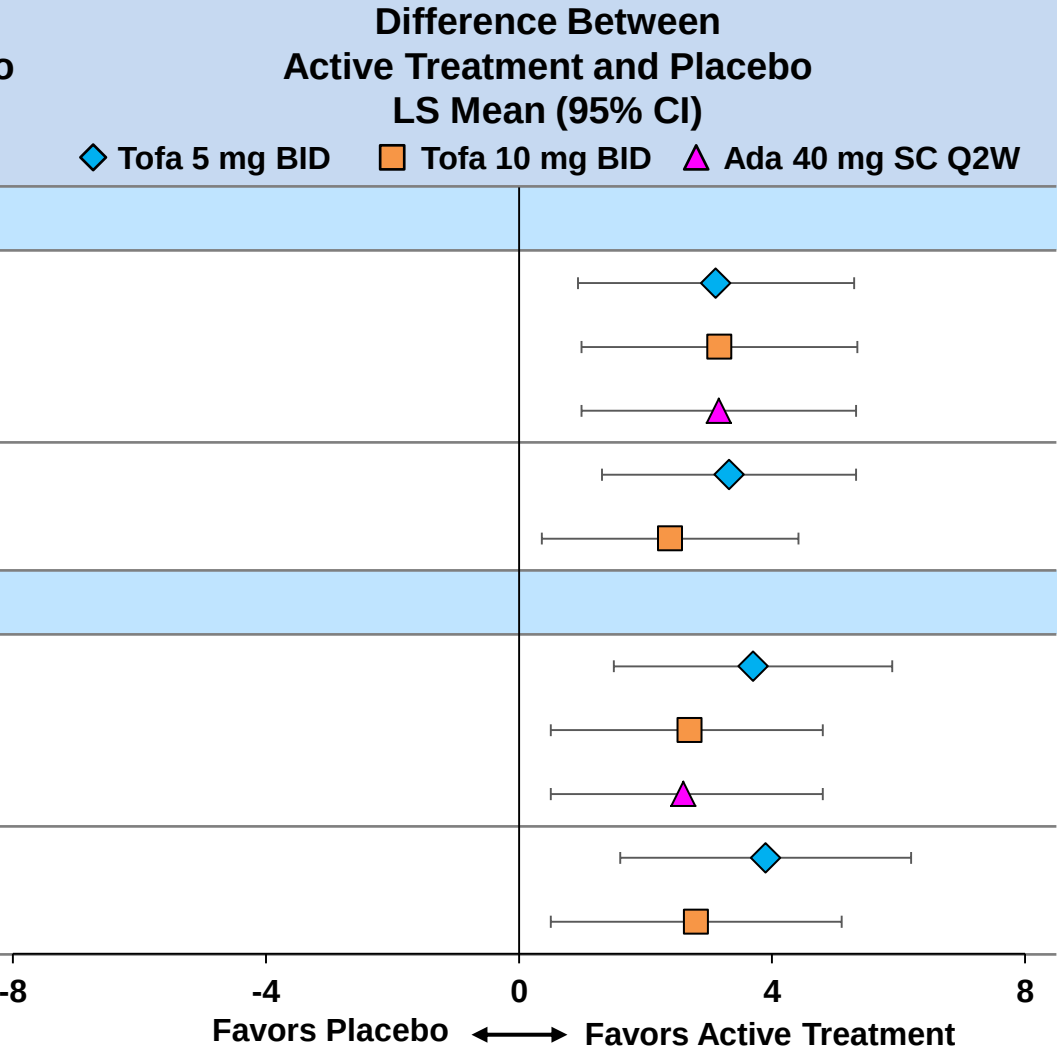


	Placebo	Tofa 5 mg BID	Tofa 10 mg BID	Ada 40 mg SC Q2W
	N	N	N	N
1091	57	60	60	58
1125	62	65	64	-

†95% CI for difference between active treatment and placebo excluded zero
For patients with Baseline DSS>0, in FAS, MMRM

Improvements in SF-36v2 Physical Functioning Domain and FACIT-F Total Score at Month 3

	Active Treatment N	Placebo N
ΔSF-36v2 Physical Functioning Domain		
TNFi-Naïve (Study 1091)	106	104
	104	104
	106	104
TNFi-IR (Study 1125)	128	129
	130	129
ΔFACIT-F Total Score		
TNFi-Naïve (Study 1091)	106	104
	104	104
	106	104
TNFi-IR (Study 1125)	128	129
	130	129



MMRM, FAS

Tofacitinib 5 mg BID Demonstrated Efficacy Across PsA Disease Manifestations in Both TNFi-Naïve and TNFi-IR Patient Populations

Peripheral Arthritis	▪ ACR 20/50/70 response rates ▪ ΔHAQ-DI ▪ Maintenance of structural integrity
Psoriasis	▪ Psoriasis Area and Severity Index (PASI)75 response rate
Enthesitis	▪ ΔLeeds Enthesitis Index score (LEI)
Dactylitis	▪ ΔDactylitis Severity Score

Efficacy in improving patient reported outcomes including physical functioning and fatigue

Overview of Presentation

Topic	Presenter
Introduction	Nancy McKay Director, Regulatory Affairs Pfizer Inc
Psoriatic Arthritis: A Rheumatologist's Perspective/ Unmet Medical Need	Philip Mease, MD, MACR Director, Rheumatology Research, Swedish-Providence-St. Joseph's Health Systems Clinical Professor, University of Washington School of Medicine, Seattle, WA
Tofacitinib PsA Development Program and Efficacy	Keith Kanik, MD, FACR Senior Director, Global Clinical Lead PsA Inflammation and Immunology Pfizer Inc
Tofacitinib PsA Safety	**Daniela Graham, MD** **Clinician, PsA Development Program** **Inflammation and Immunology** **Pfizer Inc**
Risk Management	Thomas Jones, MD Senior Director, Safety Risk Management Pfizer Inc
Benefit:Risk and Conclusions	Michael Corbo, PhD Senior VP, Chief Development Officer Inflammation and Immunology Pfizer Inc

Tofacitinib PsA Safety

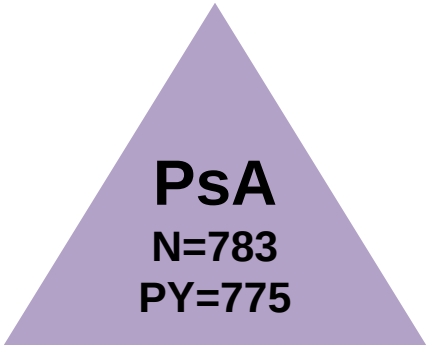
Daniela Graham, MD

Clinician, PsA Development Program

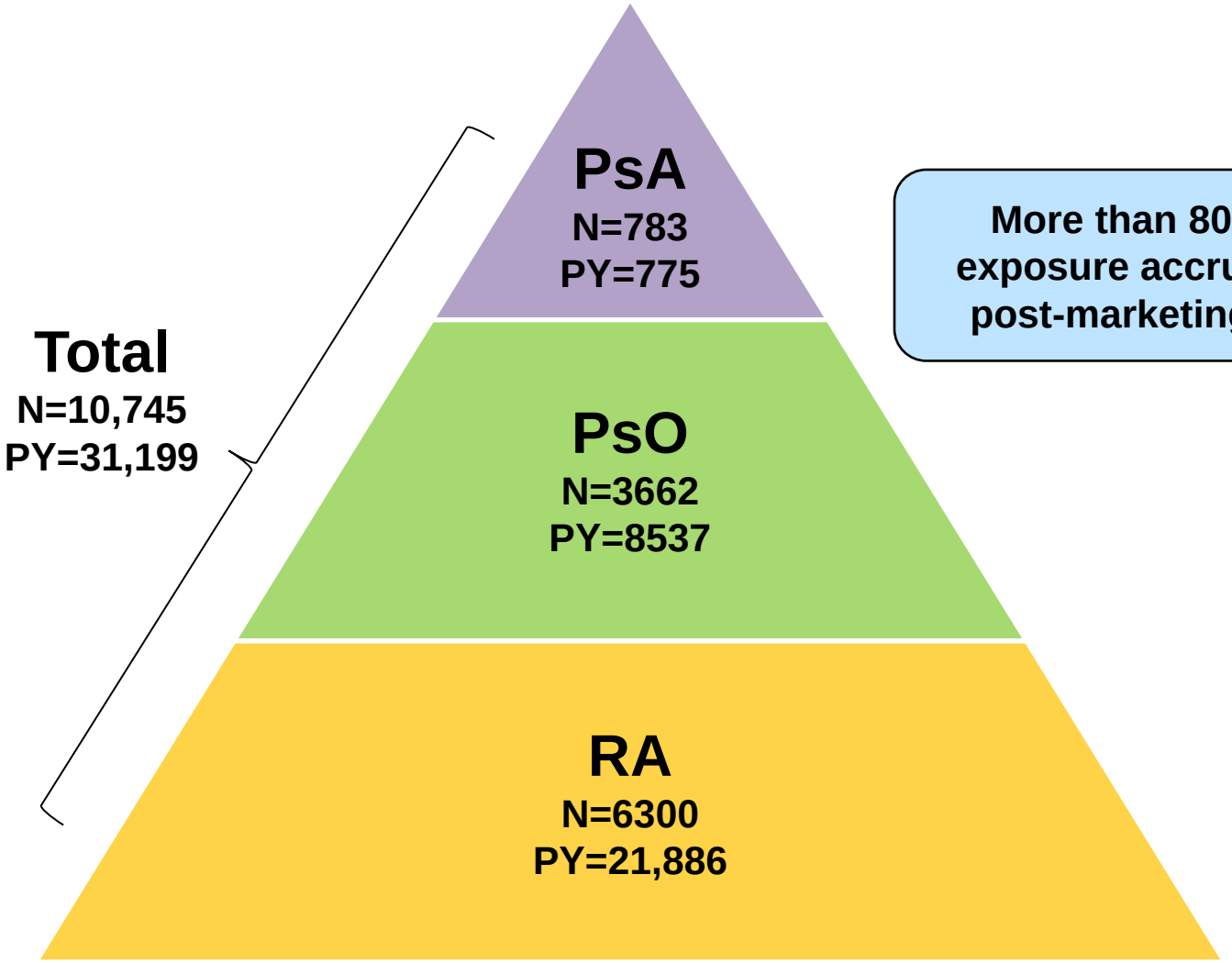
Inflammation and Immunology

Pfizer Inc

Robust Database of Patients Studied in PsA

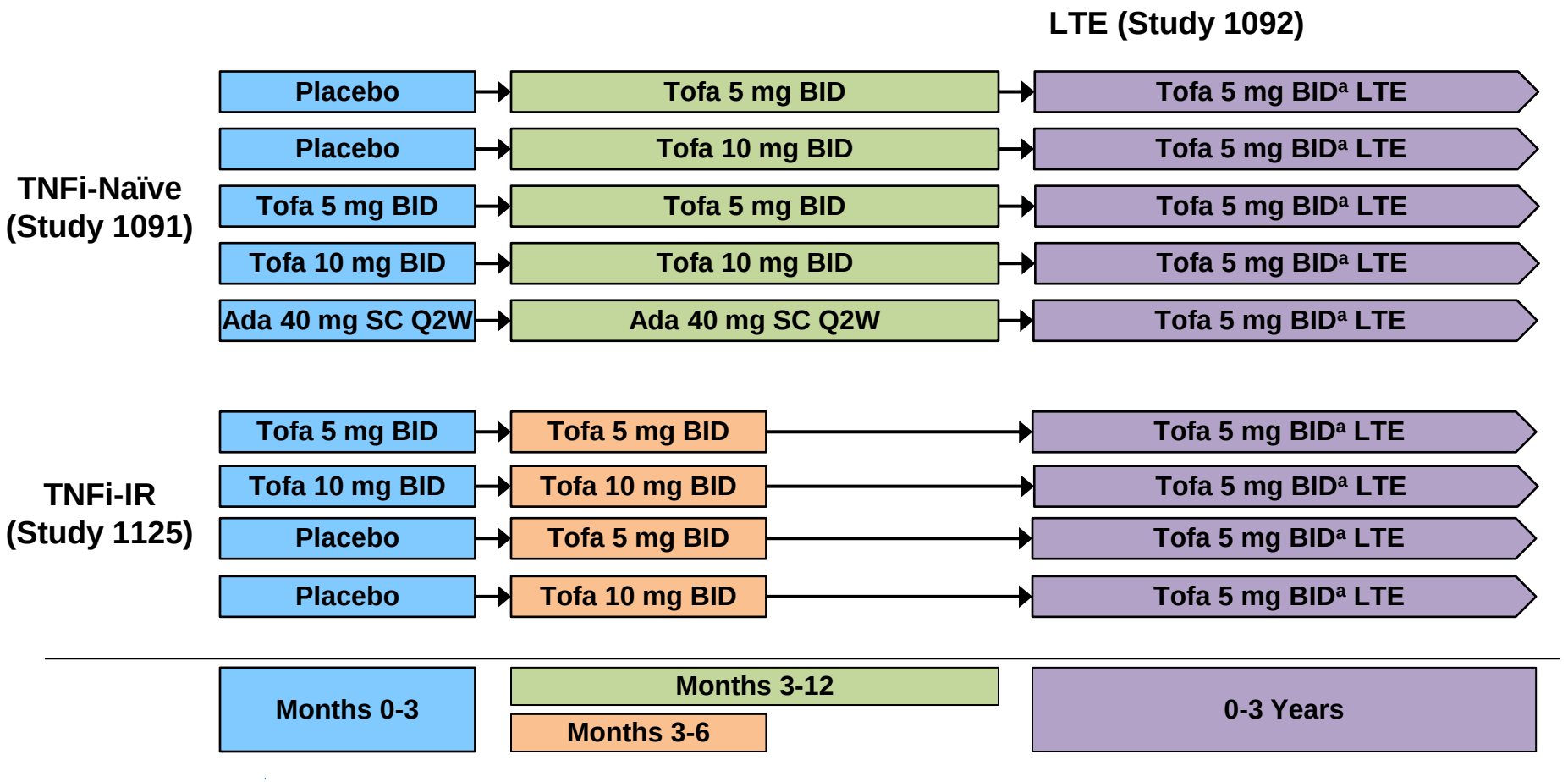


Tofacitinib Clinical Trial Patient-Years of Exposure



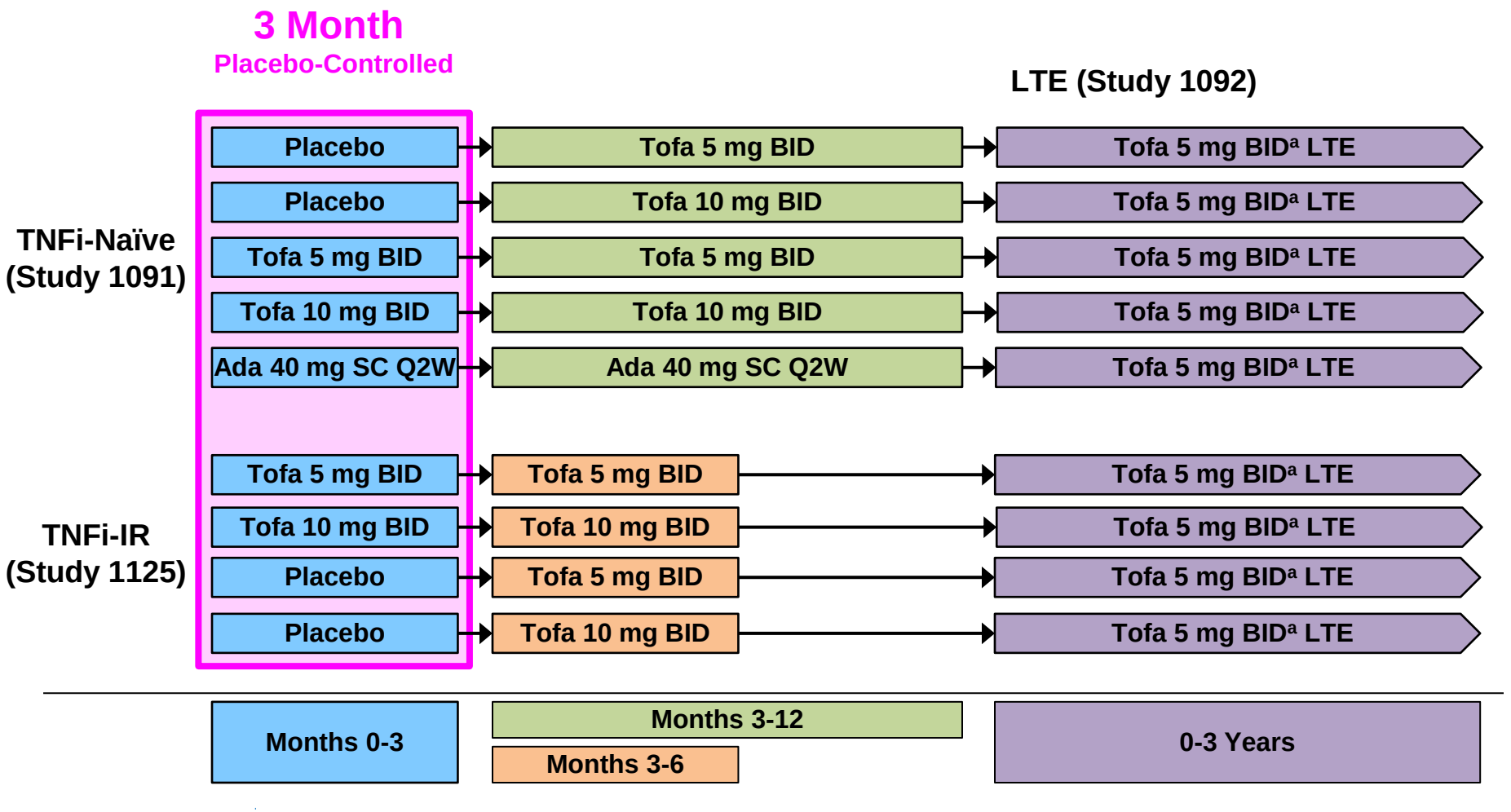
More than 80,000 PY exposure accrued in the post-marketing setting

PsA Program Structure



a. The investigator had the option to increase the dose to tofacitinib 10 mg BID in those subjects who were receiving tofacitinib 5 mg BID and, in the investigator's opinion, had PsA symptoms that are not adequately controlled. Changes in the dose were only permitted at scheduled study visits, unless a reduction to tofacitinib 5 mg BID was required due to safety abnormalities

PsA Program Structure



a. The investigator had the option to increase the dose to tofacitinib 10 mg BID in those subjects who were receiving tofacitinib 5 mg BID and, in the investigator's opinion, had PsA symptoms that are not adequately controlled. Changes in the dose were only permitted at scheduled study visits, unless a reduction to tofacitinib 5 mg BID was required due to safety abnormalities

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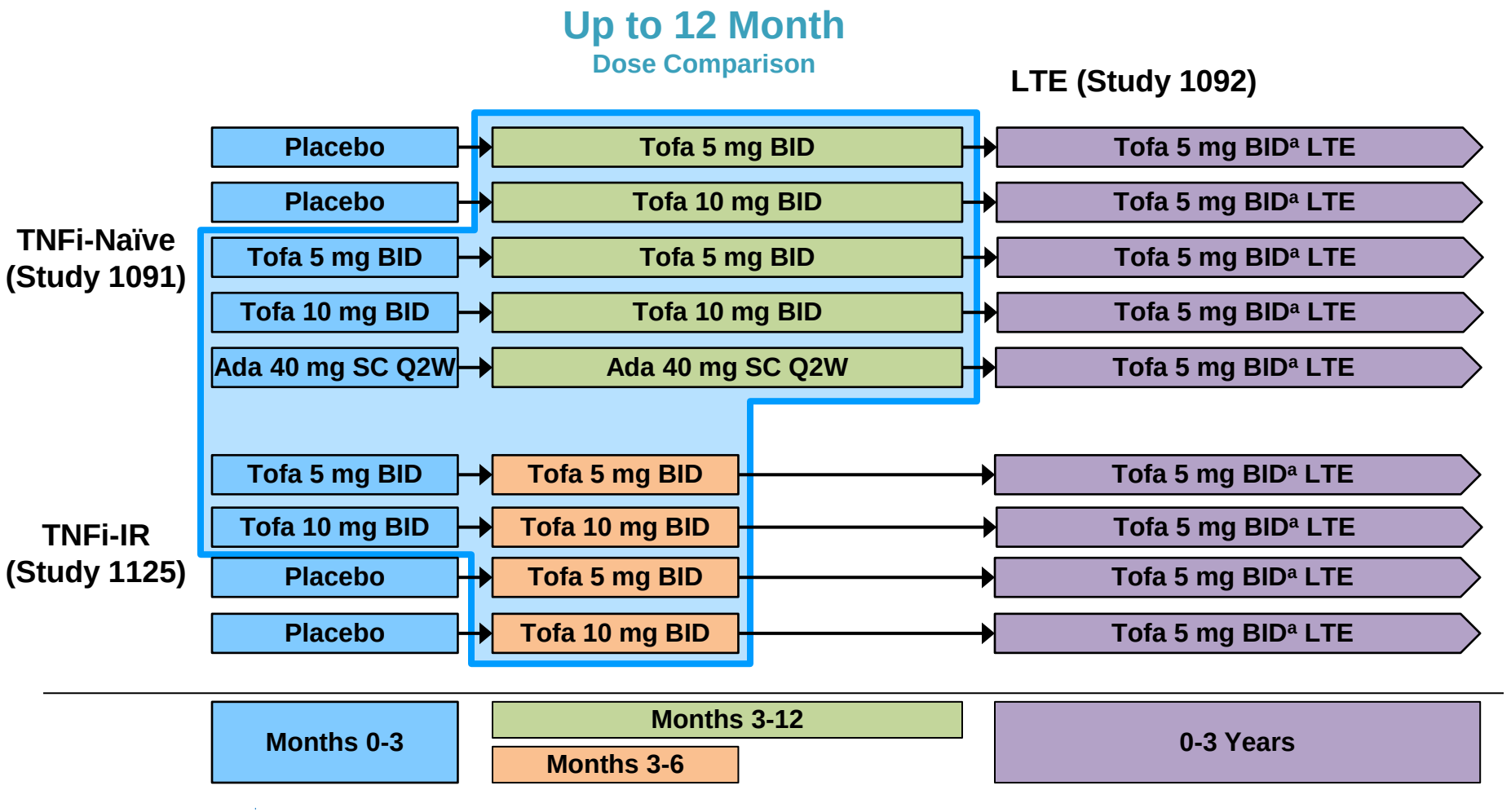

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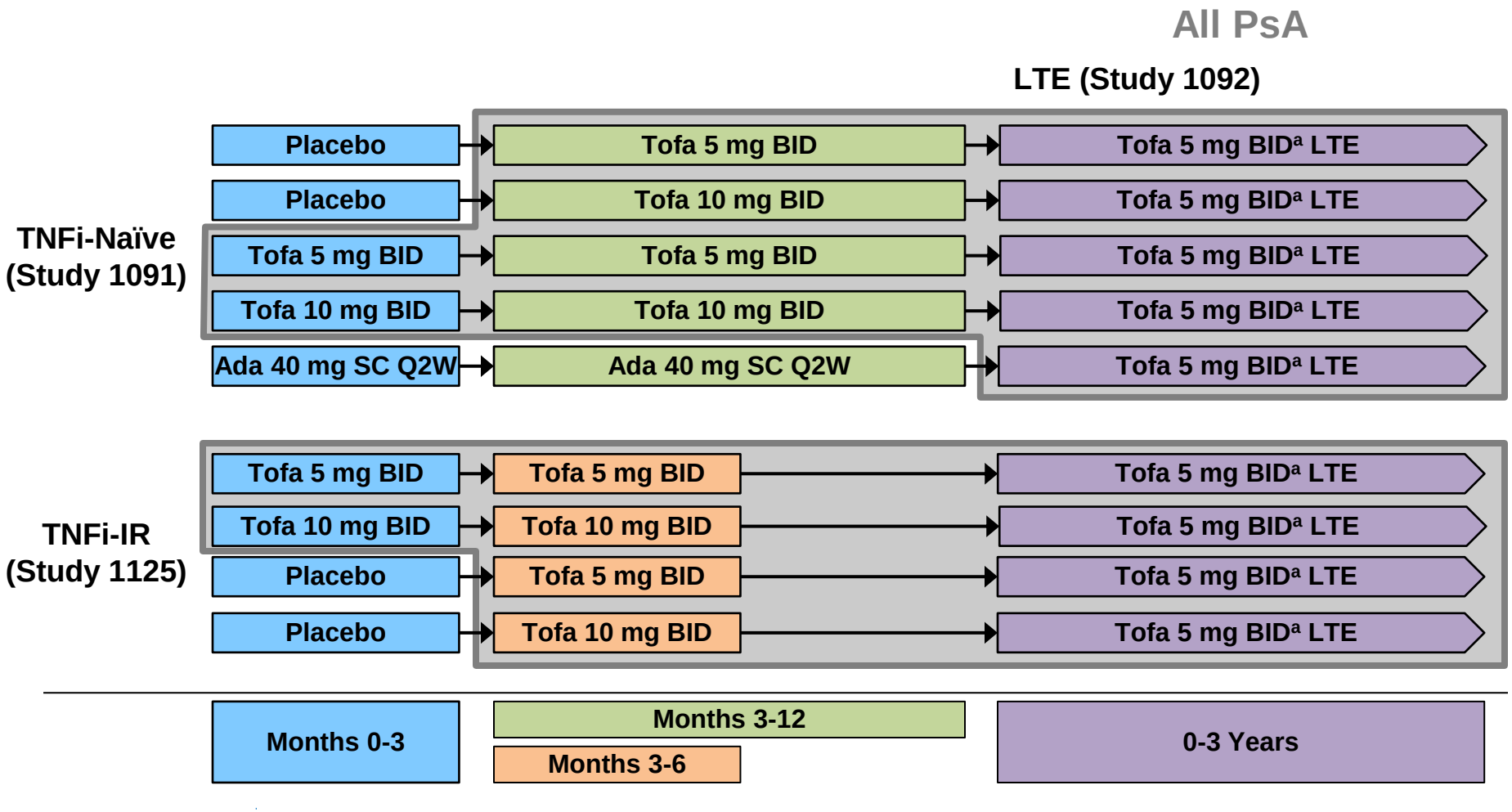

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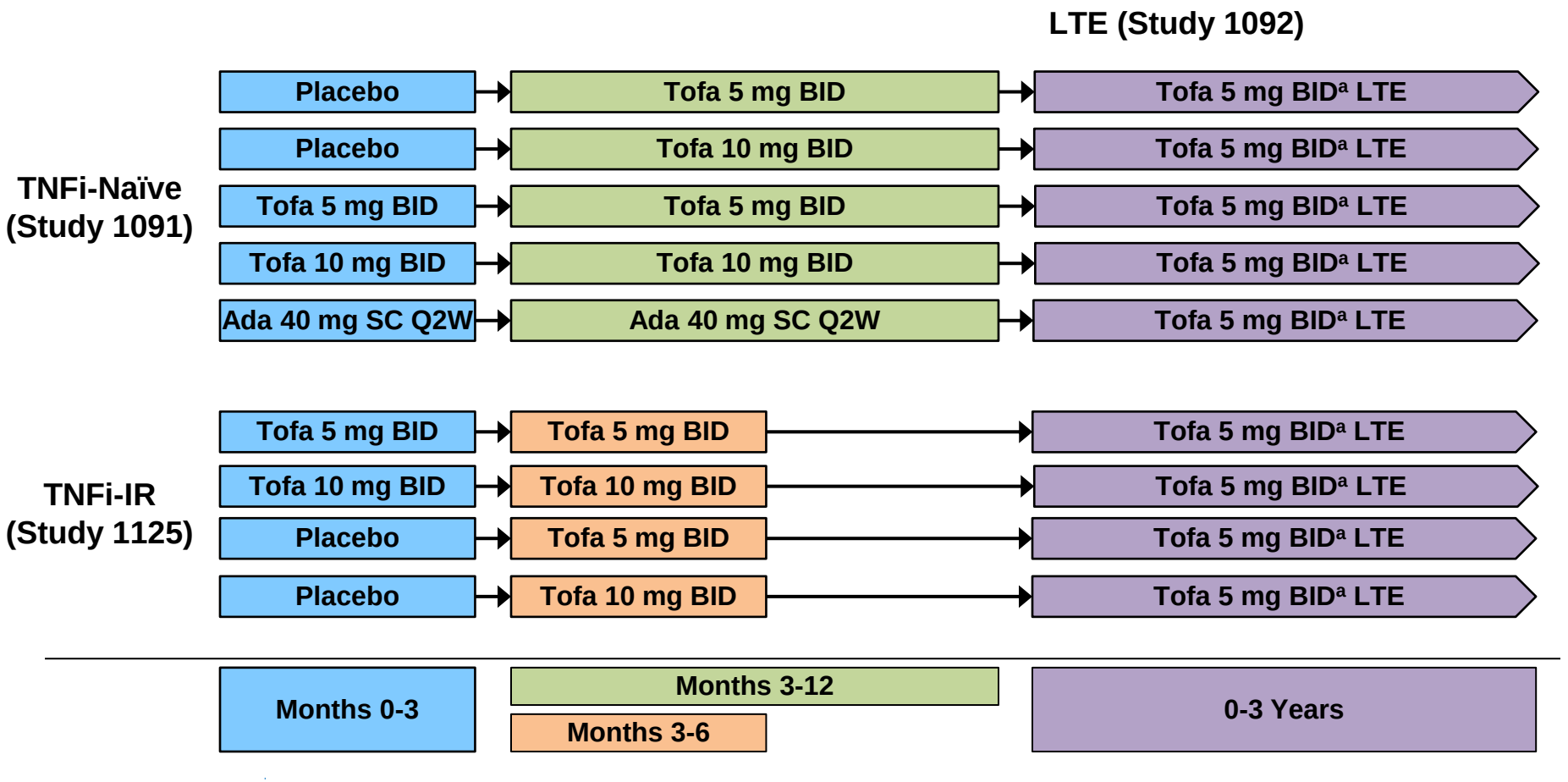

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Discontinuations During the 3 Month Placebo-Controlled Period (Pooled Data)

	Placebo N=236 n (%)	Tofa 5 mg BID N=238 n (%)	Tofa 10 mg BID N=236 n (%)	Ada 40 mg SC Q2W (Study 1091 Only) N=106 n (%)
Discontinuations (any reason)	20 (8.5)	11 (4.6)	11 (4.7)	4 (3.8)
Subjects died	0	0	0	0
Adverse event	6 (2.5)	5 (2.1)	4 (1.7)	2 (1.9)
Insufficient clinical response	4 (1.7)	1 (0.4)	2 (0.8)	0
Subject no longer willing to participate in study	6 (2.5)	2 (0.8)	2 (0.8)	1 (0.9)
Other	4 (1.7)	3 (1.3)	3 (1.3)	1 (0.9)

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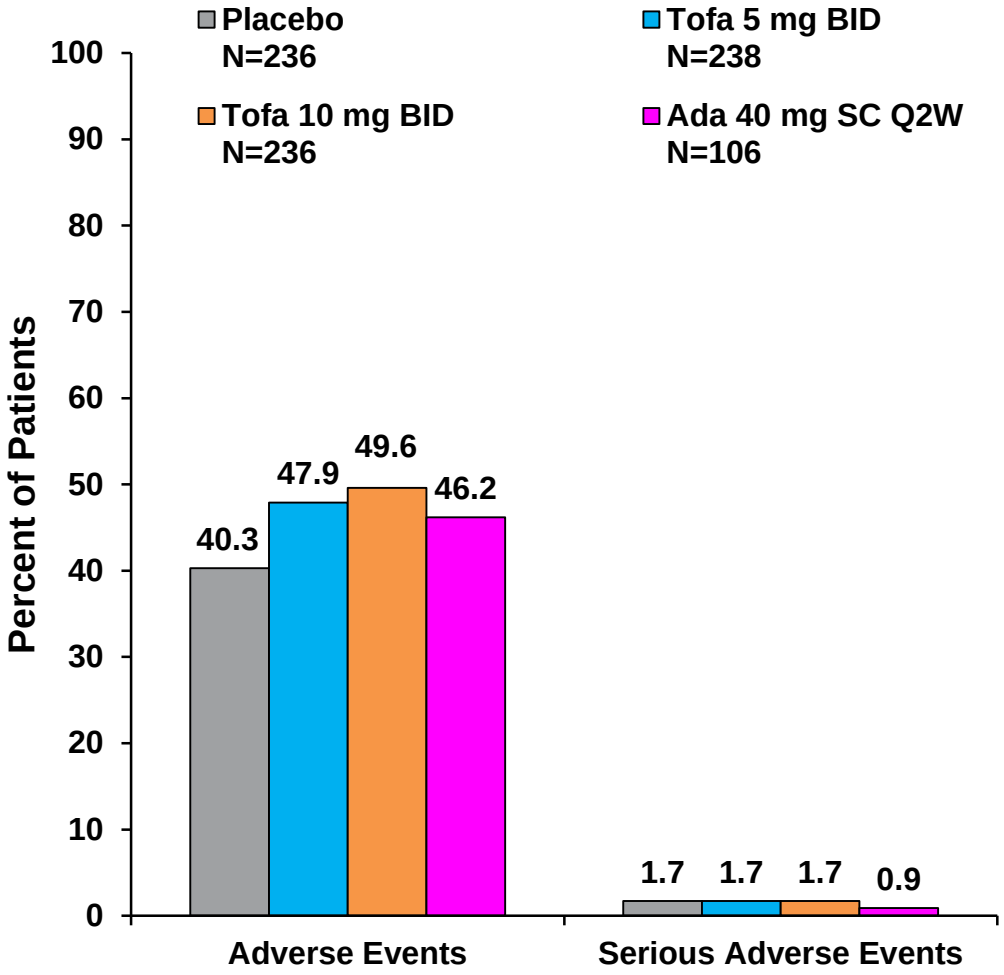
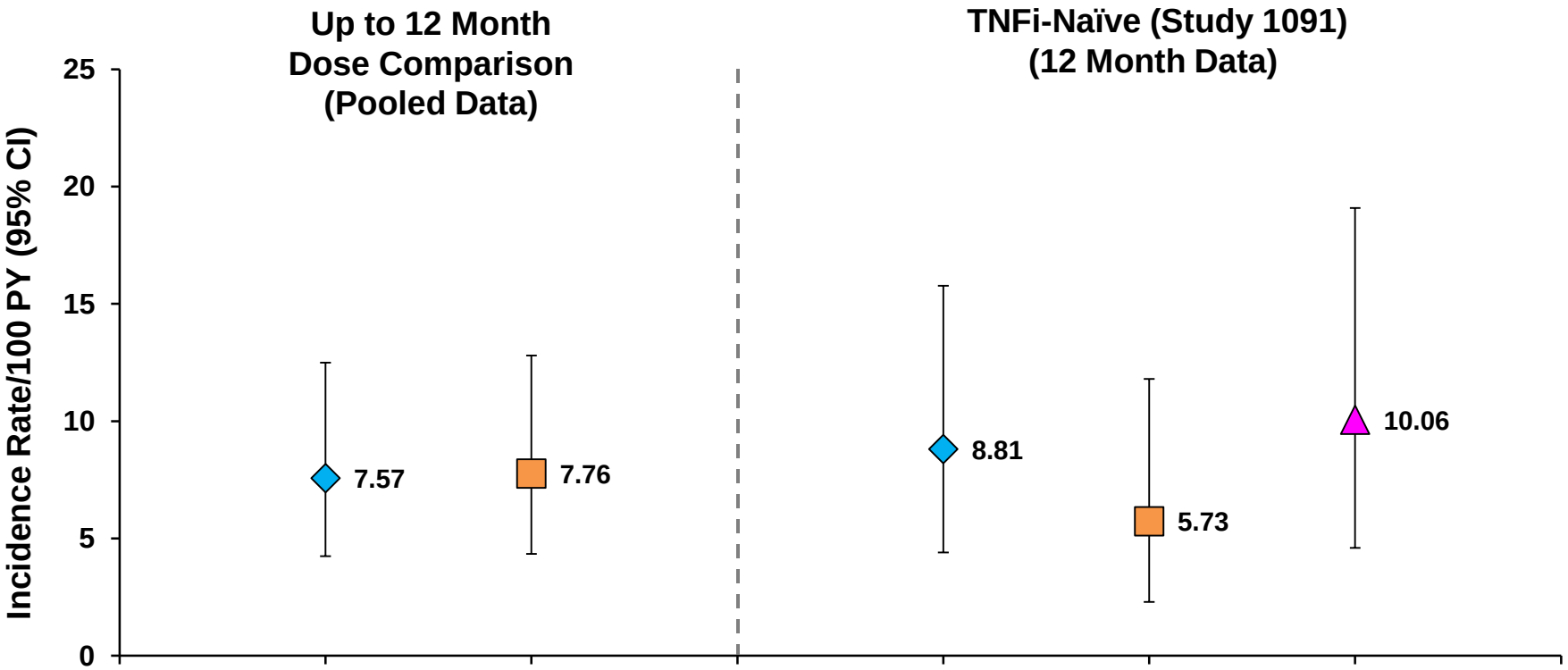
Summary of Adverse Events in the 3 Month Placebo-Controlled Period (Pooled Data)



- Most frequent AEs
  - Nasopharyngitis
  - Upper respiratory tract infections
  - Headache
- Most frequent SAEs were infections

AE=Adverse Event; SAE=Serious Adverse Event

Incidence Rate of SAEs Similar Between Tofacitinib Doses and Adalimumab



	All Tofa 5 mg BID	All Tofa 10 mg BID	All Tofa 5 mg BID	All Tofa 10 mg BID	Ada 40 mg SC Q2W
N	347	344	159	154	106
n	15	15	11	7	9
PY of Exposure	198.1	193.4	124.8	122.2	89.5

Deaths in Patients Participating in the PsA Studies (All PsA, Pooled Data)

Preferred Term	Dose at Time of Death	Randomized Sequence	Gender/ Race/ Age	Country	Days on Tofa[a]	Medical History
Sudden Cardiac Death	Tofa 5 mg BID	Placebo-Tofa 5 mg BID	Female/ White/ 73	Poland	56	• Hypertension • Diabetes • Overweight
Acute Cardiac Failure (secondary to hypertensive heart disease)	Tofa 10 mg BID	Placebo-Tofa 5 mg BID	Female/ White/ 57	UK	273	• Hypertension • Hypercholesterolemia • Recent elective surgery
Pulmonary Embolism	Tofa 5 mg BID	Tofa 5 mg BID	Female/ White/ 46	UK	346	• Obesity • Normal platelets and INR
Pancreatic Carcinoma Metastatic	Tofa 5 mg BID	Ada 40 mg SC Q2W	Male/ White/ 54	Poland	84	• Smoker

- No deaths were related to study drug, per the investigators' assessment

INR=International Normalized Ratio

Adverse Events of Special Interest

Serious Infections

Herpes Zoster

Opportunistic Infections

Major Adverse Cardiovascular Events

Malignancies

Gastrointestinal (GI) Perforations

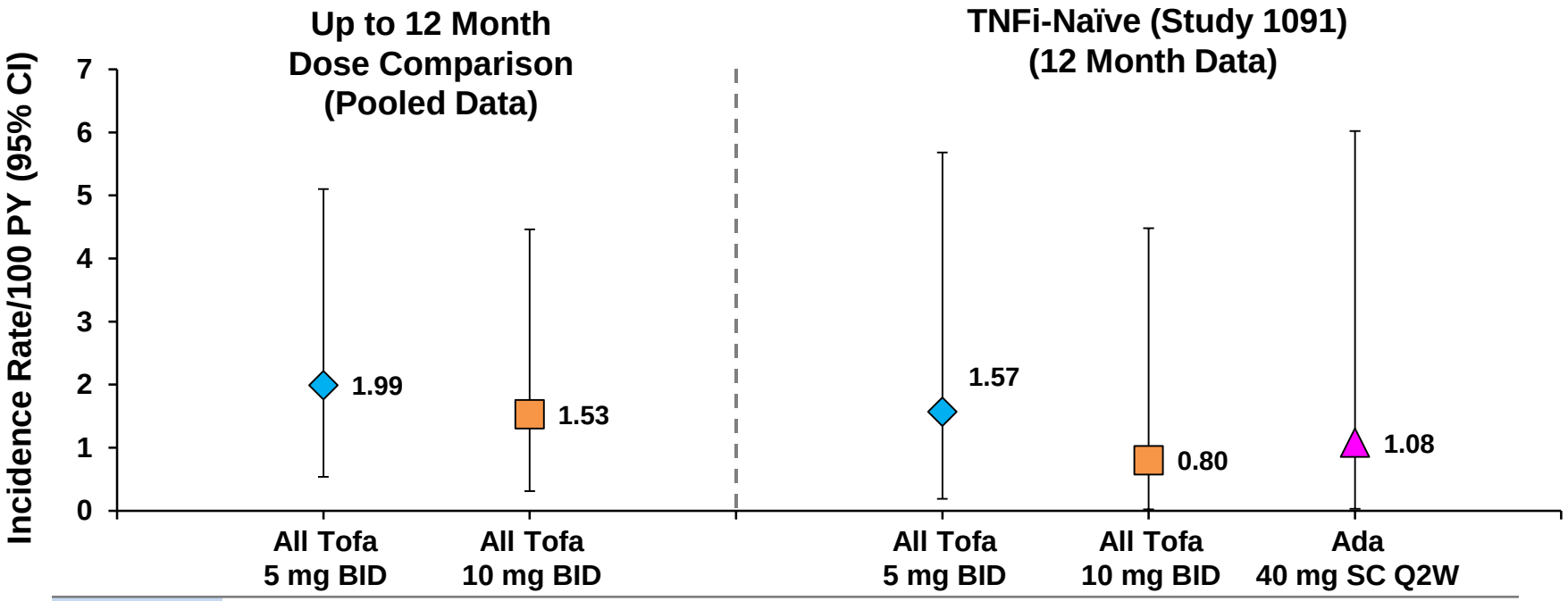
Hepatic Events

Interstitial Lung Disease

External Comparison Cohort For Risk Contextualization: Truven MarketScan Claims Database

- Observational database comprised of US medical claims
- Cohort of PsA patients in a real-world clinical setting
  - Defined as ≥1 inpatient or ≥2 outpatient diagnosis codes of PsA
  - Moderate-severe disease
  - Exclusion criteria from the tofacitinib global Phase 3 PsA studies applied
  - Included 5799 patients
- Comparison with Phase 3 trial data should be made with consideration of the differences between the two distinct data sources

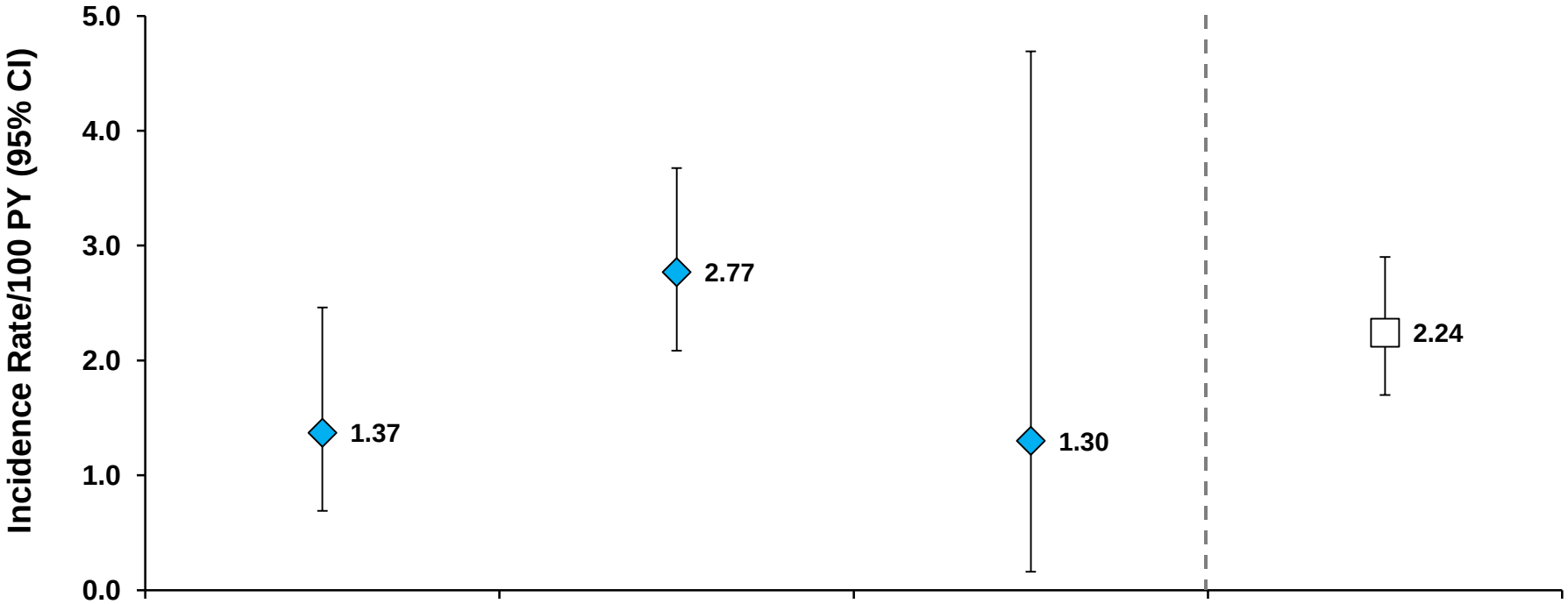
Serious Infections and Incidence Rate Similar to Adalimumab



	All Tofa 5 mg BID	All Tofa 10 mg BID	All Tofa 5 mg BID	All Tofa 10 mg BID	Ada 40 mg SC Q2W
N	347	344	159	154	106
n	4	3	2	1	1
PY of Exposure	200.7	196.5	127.1	124.3	92.6

- Serious infections were pneumonia, oral candidiasis, influenza, pyelonephritis, parotitis, herpes simplex/pyoderma streptococcal
- All resolved after treatment

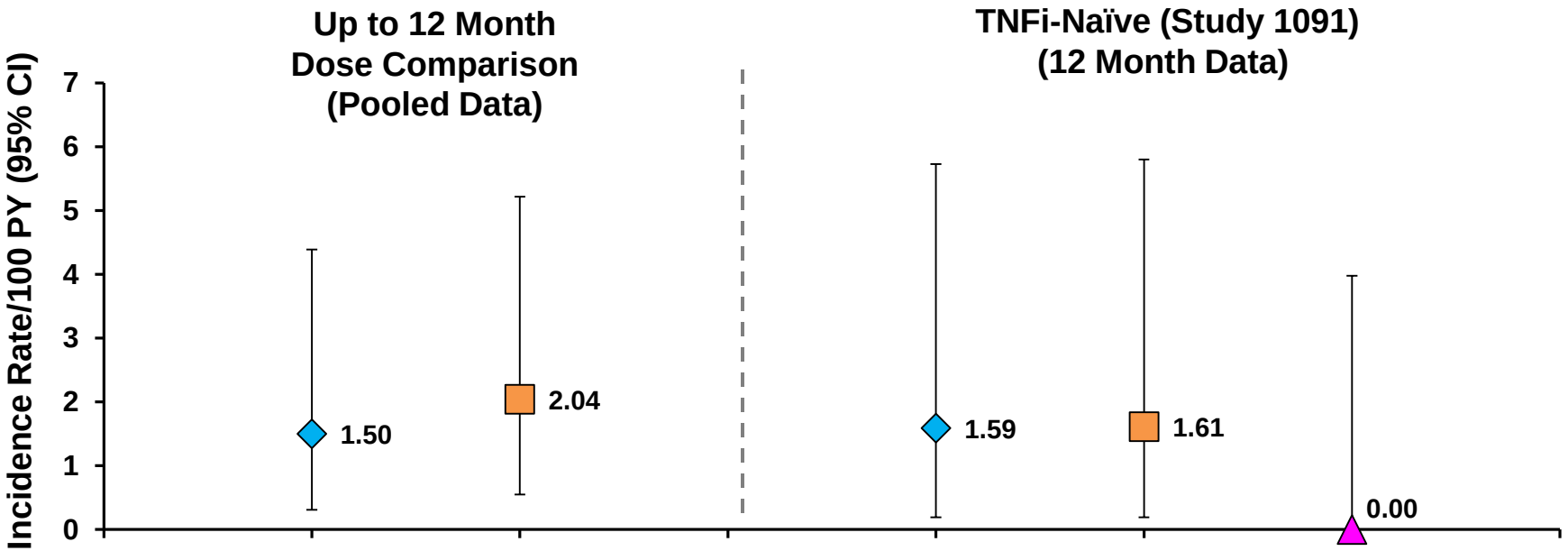
Serious Infections Incidence Rate in PsA Similar to Other Tofacitinib RCT Programs



	Psoriasis (Up to 12 Months) Tofa 5 mg BID	Rheumatoid Arthritis (Up to 24 Months) Tofa 5 mg BID	Psoriatic Arthritis (Up to 12 Months) Tofa 5 mg BID	PsA Truven[a] Any bDMARDs
N	1217	1589	238	5075
n	11	48	2	58
PY of Exposure	800.8	1733.8	154.1	2589.5

a. Hospitalizations only
RCT=Randomized Controlled Trial

Herpes Zoster Incidence Rate Similar Between Tofacitinib Doses

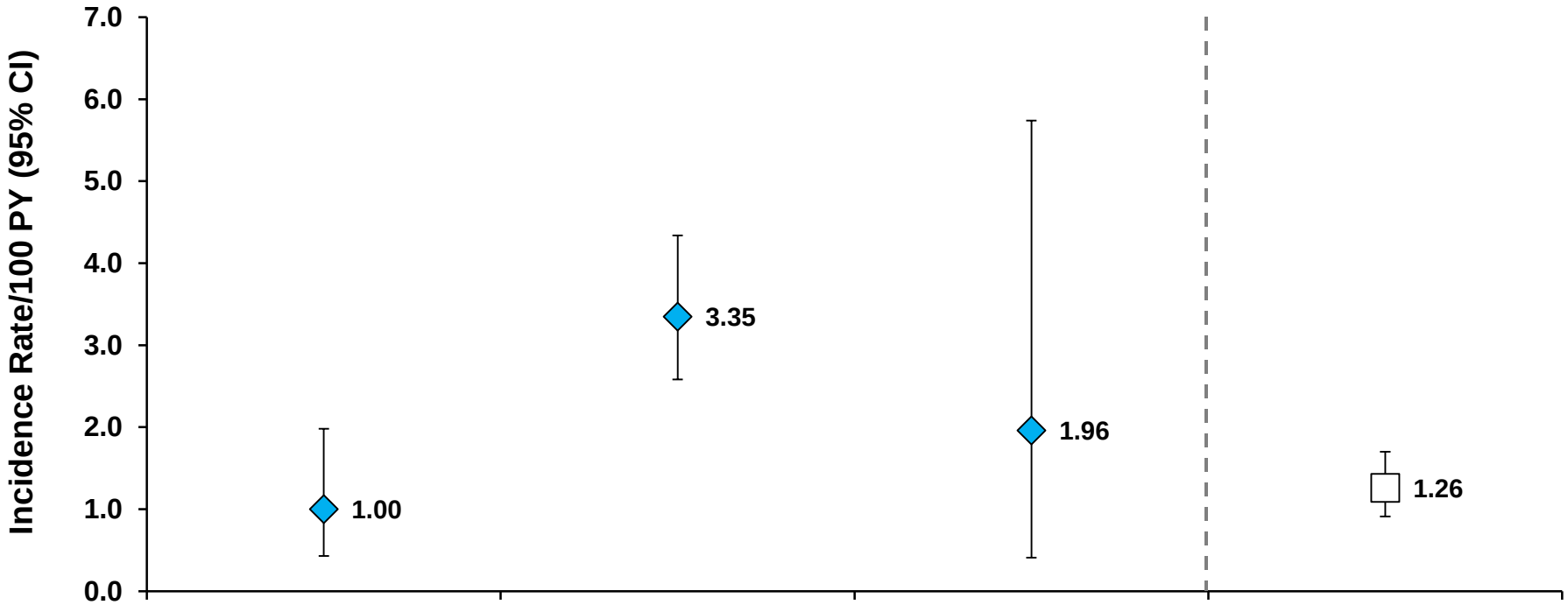


	All Tofa 5 mg BID	All Tofa 10 mg BID	All Tofa 5 mg BID	All Tofa 10 mg BID	Ada 40 mg SC Q2W
N	347	344	159	154	106
n	3	4	2	2	0
PY of Exposure	199.6	196.4	126.0	124.5	92.6

- One case was a multidermatomal HZ and was considered an opportunistic infection

HZ=Herpes Zoster

Herpes Zoster Incidence Rate in PsA Similar to Those in Other Tofacitinib RCT Programs



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N	1217	1589	238	5075
n	8	57	3	42
PY of Exposure	800.8	1702.7	152.7	3343.0

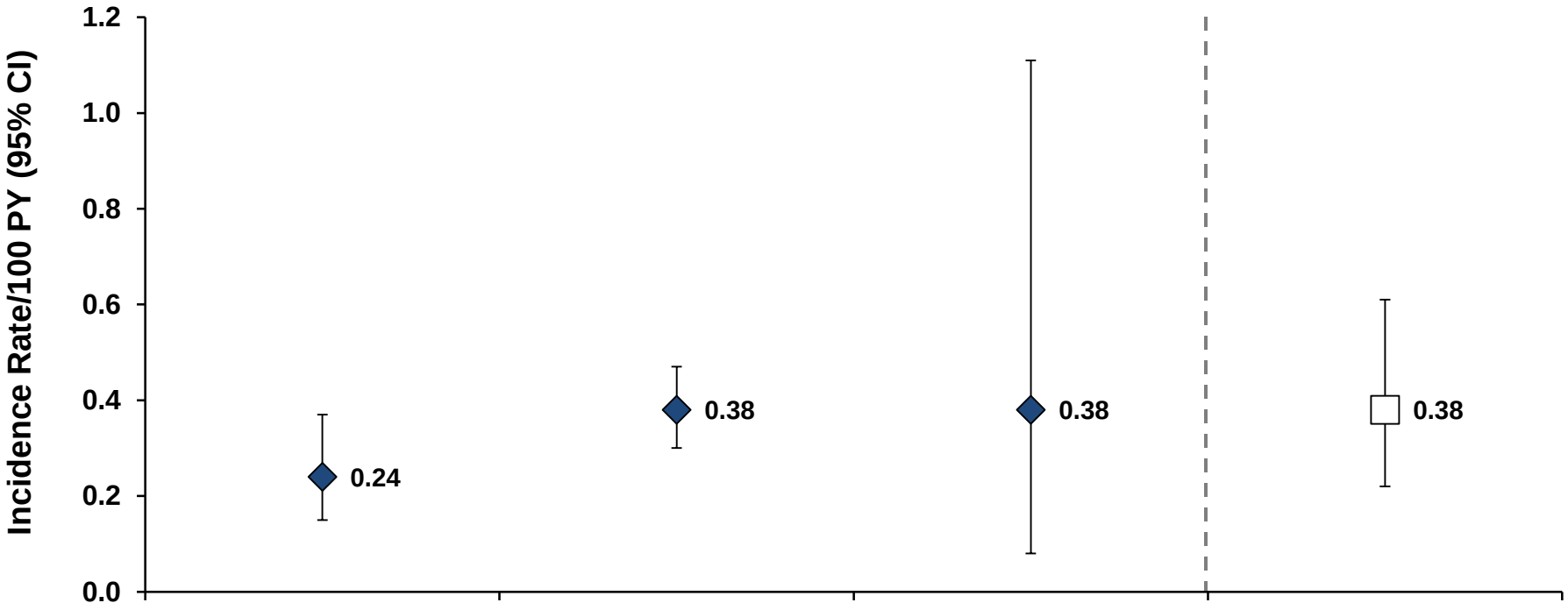
Incidence of Major Adverse Cardiovascular Events (All PsA, Pooled Data)

- Major Adverse Cardiovascular Events (MACE)
  - MACE is a composite CV endpoint comprised of cardiovascular deaths and non-fatal CV events of myocardial infarction and cerebrovascular events

- 3 cases of MACE
  - Sudden cardiac death
  - Non-fatal MI
  - Non-fatal ischemic stroke

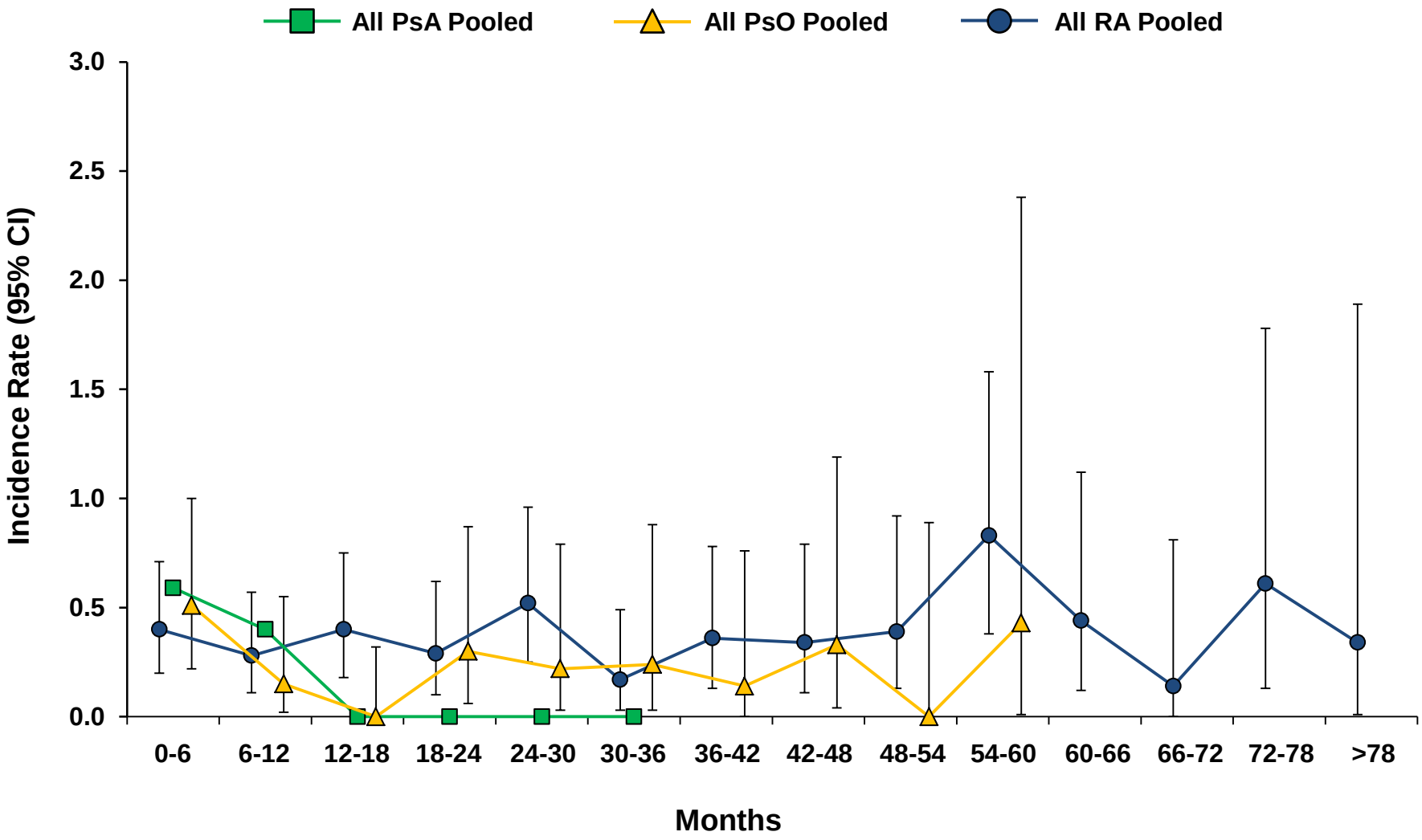
CV=Cardiovascular; MI=Myocardial Infarction

MACE Incidence Rate in PsA is Similar to Other Tofacitinib Long Term Study Data



	Psoriasis (All PsO) All Tofa Doses	Rheumatoid Arthritis (All RA) All Tofa Doses	Psoriatic Arthritis (All PsA) All Tofa Doses	Truven Any bDMARDs (PsA)
N	3662	5856	783	5057
n	21	80	3	17
PY of Exposure	8759.3	21,285.9	790.5	4467.8

Incidence Rates for MACE Risk Over Time (All PsA and PsO Pooled, and RA)



Confidence intervals for PsA data are not shown

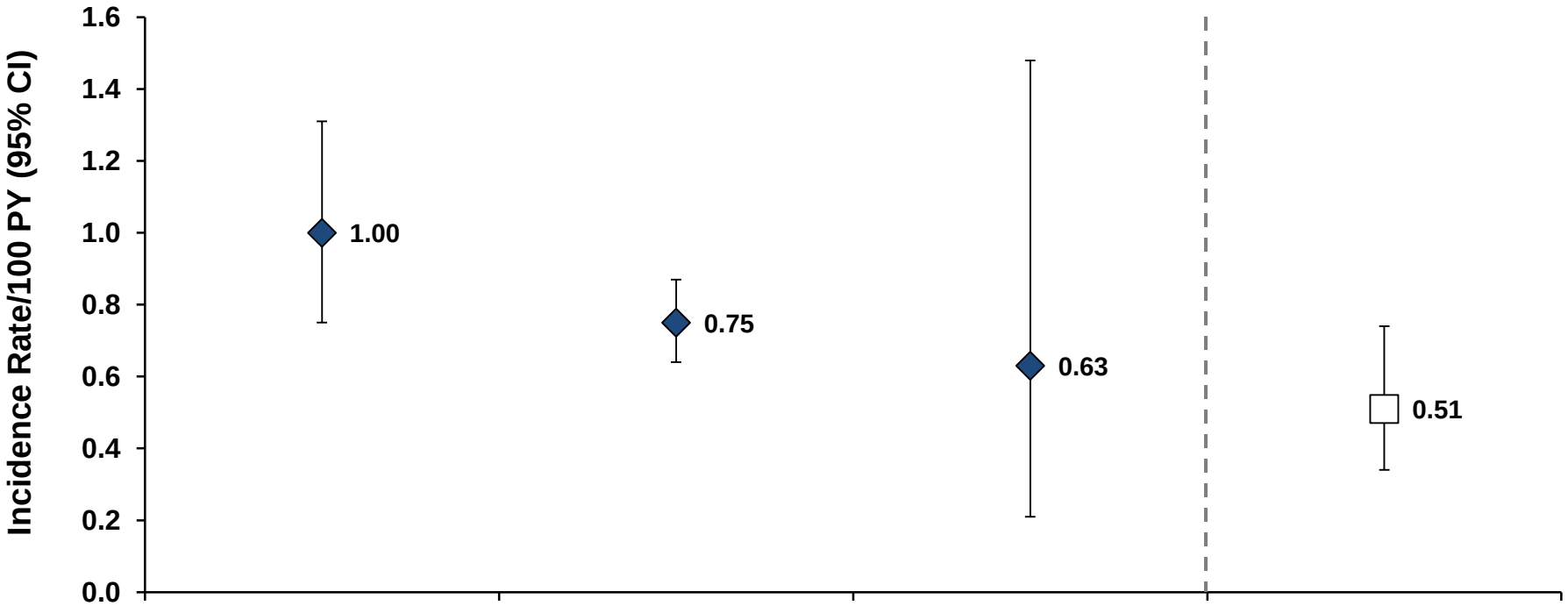
Malignancies Excluding NMSC (All PsA, Pooled Data)

Malignancy Type	Randomization Sequence	LTE	Dose at Time of Onset	Gender/ Race/ Age[a]	Country	Days on Tofacitinib	Comments
Urothelial carcinoma	Tofa 5 mg BID	No	Tofa 5 mg BID	Male/ White/ 58	Poland	48	Hematuria at baseline
Renal cell carcinoma	Ada 40 mg SC Q2W	Yes	Tofa 5 mg BID	Male/ Other/ 44	Mexico	32	Smoker
Pancreatic duct adenocarcinoma metastatic	Ada 40 mg SC Q2W	Yes	Tofa 5 mg BID	Male/ White/ 52	Poland	84	Smoker
Squamous cell carcinoma of the vulva	Tofa 5 mg BID	No	Tofa 5 mg BID	Female/ White/ 65	Mexico	65	Abnormal urinalysis since Study Day 11
Breast ductal carcinoma	Tofa 5 mg BID	No	Tofa 5 mg BID	Female/ White/ 67	USA	244	Postmenopausal, Biopsy: ER (+), PgR (+), HER2 (-), Stage II

a. Age at screening

ER=Estrogen Receptors; HER2=Human Epidermal growth factor Receptor 2; NMSC=Non-Melanoma Skin Cancer; PgR=Progesterone Receptor

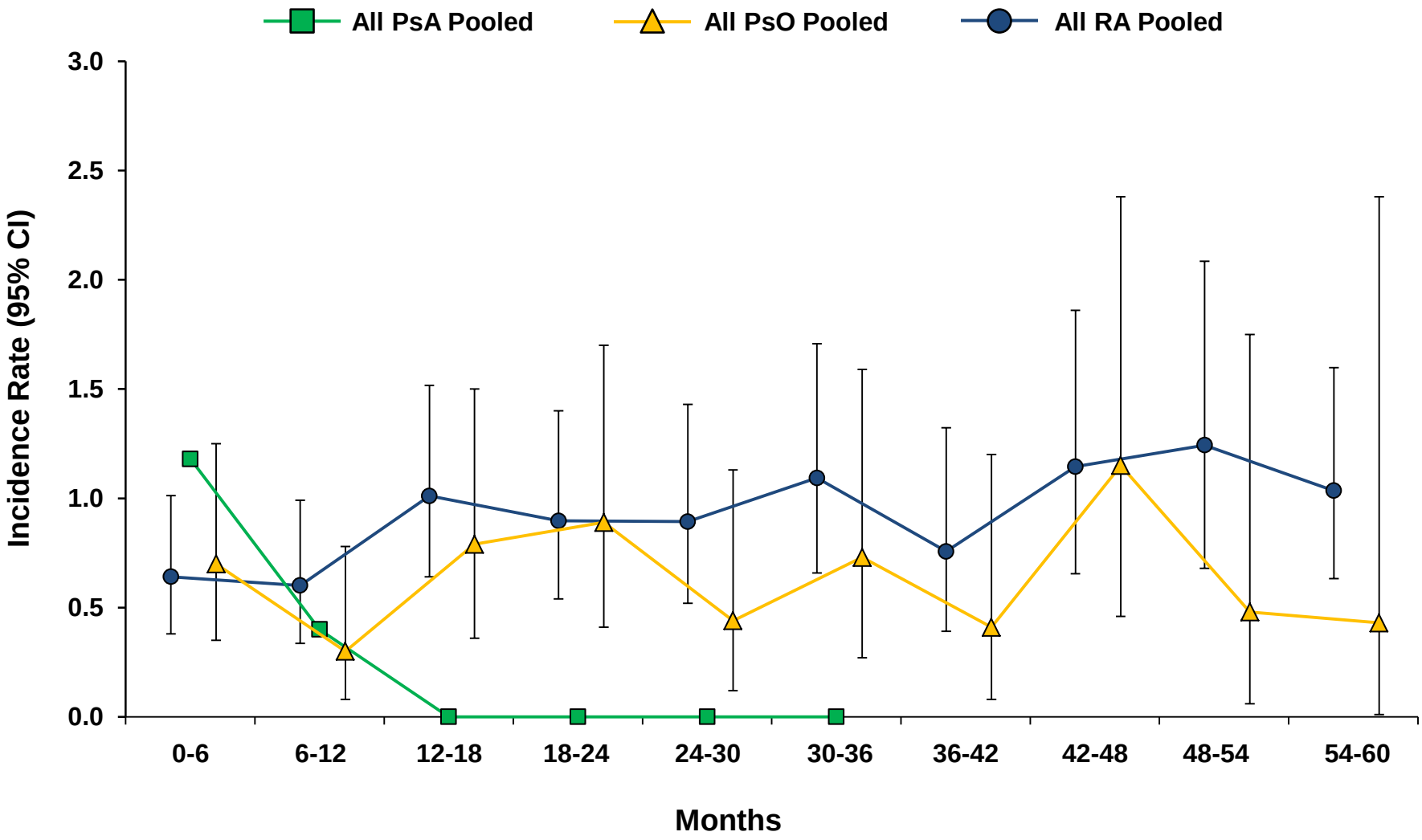
Malignancies (Excl. NMSC) Incidence Rate in PsA within Range of Those Reported in Other Tofacitinib Long Term Study Data



	Psoriasis (All PsO) All Tofa Doses	Rheumatoid Arthritis (All RA) All Tofa Doses	Psoriatic Arthritis (All PsA) All Tofa Doses	Truven Any bDMARDs (PsA)
N	3623	6300	783	5075
n	52	168	5	28
PY of Exposure	5203.6	22,353.7	790.5	5499.1

Excl.=Excluding

Rate of Malignancies (Excl. NMSC) Over Time (All PsA and PsO Pooled, and RA)

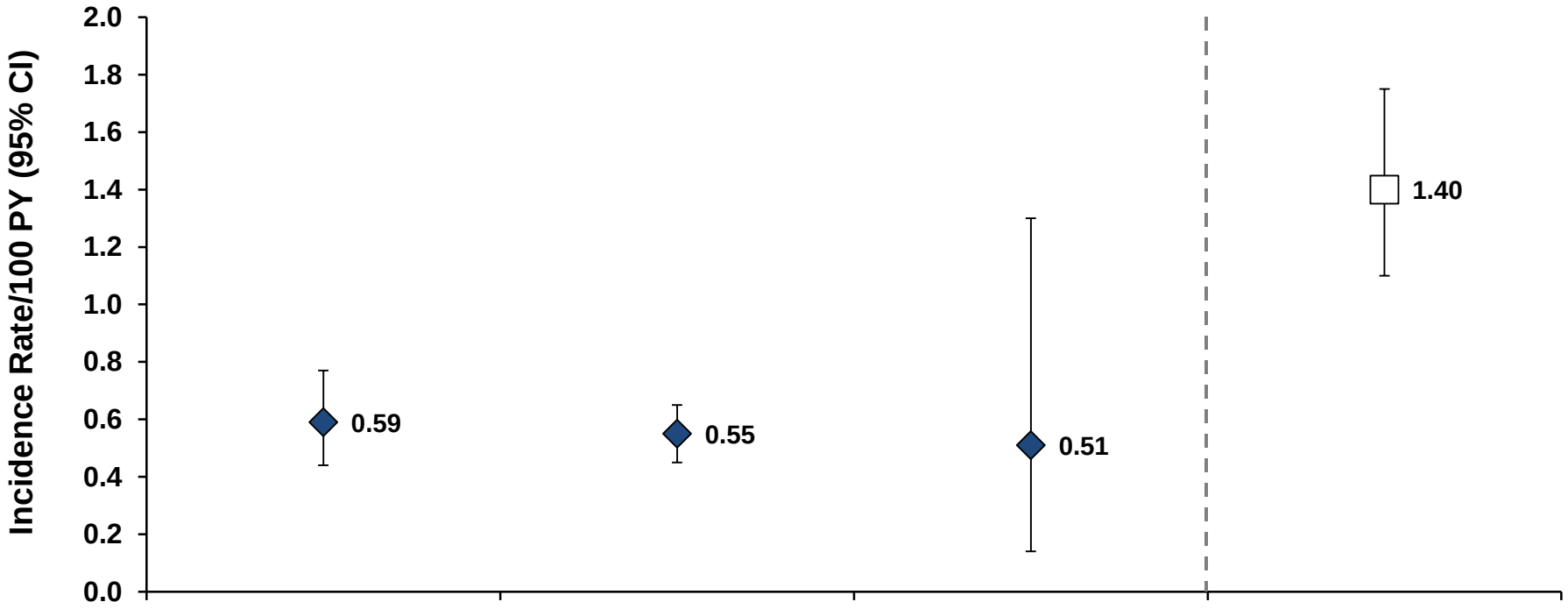


Confidence intervals for PsA data are not shown

Incidence of Non-Melanoma Skin Cancer (All PsA, Pooled Data)

- Basal cell carcinoma (n=2)
- Squamous cell carcinoma (n=2)
- All cases occurred in sun exposed areas of fair skinned individuals

NMSC Incidence Rate in PsA are within Range of Those Reported in Other Programs (All PsA, Pooled Data)



	Psoriasis (All PsO) All Tofa Doses	Rheumatoid Arthritis (All RA) All Tofa Doses	Psoriatic Arthritis (All PsA) All Tofa Doses	Truven Any bDMARDs (PsA)
N	3662	6300	783	5075
n	51	121	4	76
PY of Exposure	8689.7	22,131.5	789.2	5447.8

Laboratory Parameters Showed Similar Trends to Those Observed in Other Programs

- Modest dose dependent decreases in neutrophils and hemoglobin
  - Absolute neutrophil counts were not associated with an increased incidence of infections
- Modest decreases in the absolute lymphocyte counts in the long term extension study
- Modest dose dependent increases in high density lipoprotein (HDL) and low density lipoprotein (LDL)
- Transaminase changes
  - Liver transaminase elevations >3X ULN were infrequent and not dose-dependent
  - One patient had ≥5X ULN elevation of ALT
  - No patients with ≥10X ULN
- Modest dose dependent increases in serum creatinine

ALT=Alanine Aminotransferase

Other AEs of Special Interest (All PsA, Pooled Data)

- Gastrointestinal perforations
  - 1 event of appendicitis with perforation
- Interstitial lung disease
  - No events
- Tuberculosis
  - No events
- Hepatic events
  - No events of hepatic failure, fibrosis or cirrhosis
  - No subjects met Hy's Law criteria

Overarching Safety Conclusions

- Safety profile of tofacitinib is well characterized, stable and manageable

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Overarching Safety Conclusions

- Safety profile of tofacitinib is well characterized, stable and manageable
- No new signals have been identified in the PsA program
- Rates of adverse events of special interest in the PsA program are similar to those observed in biologic DMARDs (except herpes zoster)
- Safety profile in the PsA program is consistent with those observed in the RA and PsO safety databases

Overview of Presentation

Topic	Presenter
Introduction	Nancy McKay Director, Regulatory Affairs Pfizer Inc
Psoriatic Arthritis: A Physician's Perspective/ Unmet Medical Need	Philip Mease, MD, MACR Director, Rheumatology Research, Swedish-Providence-St. Joseph Health Systems Clinical Professor, University of Washington School of Medicine, Seattle, WA
Tofacitinib PsA Development Program and Efficacy	Keith Kanik, MD, FACR Senior Director, Global Clinical Lead PsA Inflammation and Immunology Pfizer Inc
Tofacitinib PsA Safety	Daniela Graham, MD Clinician, PsA Development Program Inflammation and Immunology Pfizer Inc
Risk Management	**Thomas Jones, MD** **Senior Director, Safety Risk Management** **Pfizer Inc**
Benefit:Risk and Conclusions	Michael Corbo, PhD Senior VP, Chief Development Officer Inflammation and Immunology Pfizer Inc

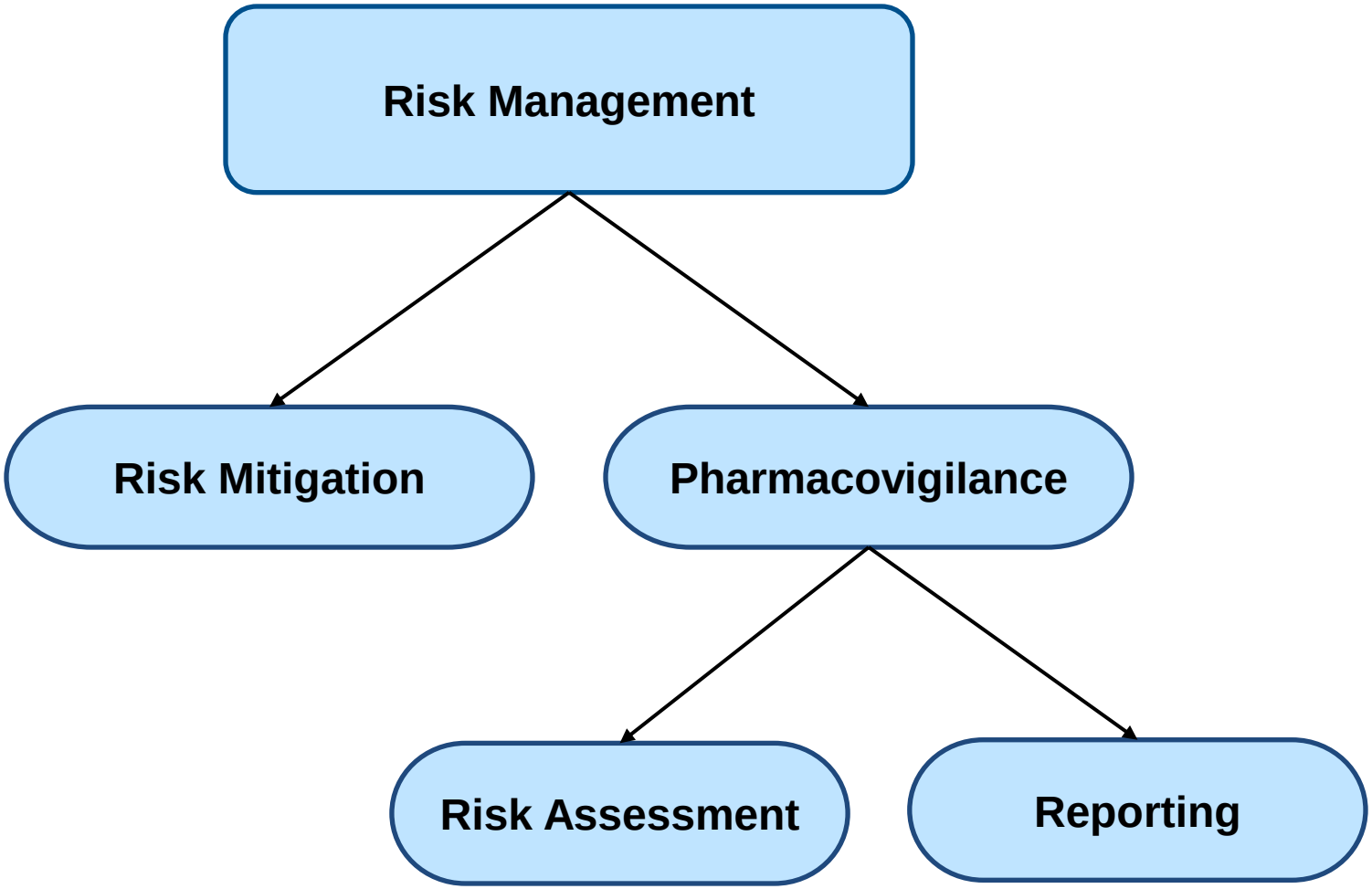
Risk Management

Thomas Jones, MD

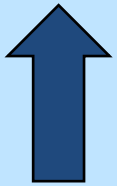
Senior Director, Safety Risk Management

Pfizer Inc

Effective Approach to Risk Management for Tofacitinib



Risk Management for Tofacitinib in PsA: Building on Effective Approach in RA and Consistent Safety Profile

Risks and Other Safety Information	Mitigation
Serious infections including TB, viral reactivation	 Risk mitigation through product labeling proposed for PsA same as for RA 
Malignancy including LPD	
NMSC	
GI Perforations	
Abnormal labs (lymphocytes, neutropenia, anemia, liver enzyme and lipid elevations)	
Vaccinations (avoid use of live vaccines while on tofacitinib)	
Drug-drug interactions (DDI), concomitant immunosuppressants	
Specific populations (pregnancy, pediatric, geriatric, diabetic, renal and hepatic impairment)	

LPD=Lympho-Proliferative Disorders; TB=Tuberculosis

Risk Management for Tofacitinib in PsA: Building on Effective Approach in RA and Consistent Safety Profile

Risks and Other Safety Information	Mitigation	Pharmacovigilance: Assessment and Reporting
		Routine Monitoring/ Reporting
Serious infections including TB, viral reactivation	Risk mitigation through product labeling proposed for PsA same as for RA	√
Malignancy including LPD		√
NMSC		√
GI Perforations		√
Abnormal labs (lymphocytes, neutropenia, anemia, liver enzyme and lipid elevations)		√
Vaccinations (avoid use of live vaccines while on tofacitinib)		√
Drug-drug interactions (DDI), concomitant immunosuppressants		√
Specific populations (pregnancy, pediatric, geriatric, diabetic, renal and hepatic impairment)		√

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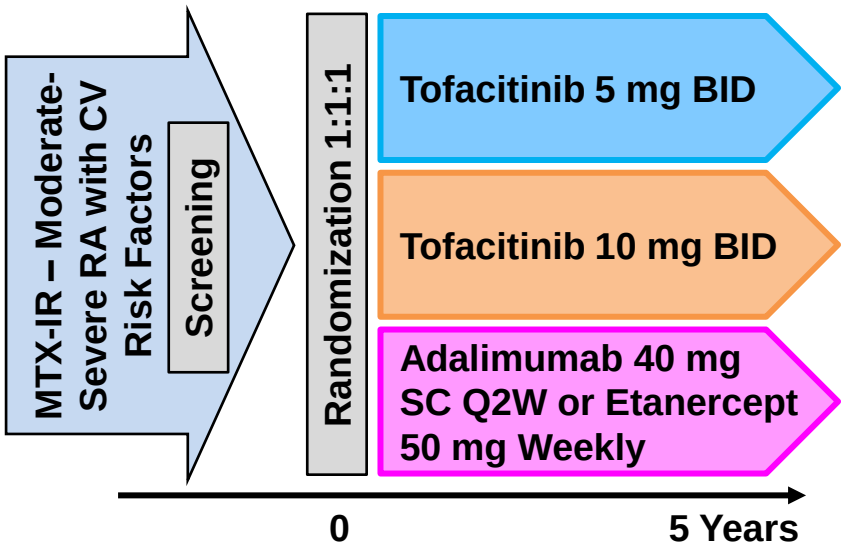
Risk Management for Tofacitinib in PsA: Building on Effective Approach in RA and Consistent Safety Profile

Risks and Other Safety Information	Mitigation	Pharmacovigilance: Assessment and Reporting		
		Routine Monitoring/ Reporting	Study 1092 PsA LTE Study	Indirectly via RA Studies
Serious infections including TB, viral reactivation	Risk mitigation through product labeling proposed for PsA same as for RA	√	√	√
Malignancy including LPD		√	√	√
NMSC		√	√	√
GI Perforations		√	√	√
Abnormal labs (lymphocytes, neutropenia, anemia, liver enzyme and lipid elevations)		√	√	√
Vaccinations (avoid use of live vaccines while on tofacitinib)		√	√	√
Drug-drug interactions (DDI), concomitant immunosuppressants		√	√	√
Specific populations (pregnancy, pediatric, geriatric, diabetic, renal and hepatic impairment)		√	√	Pregnancy registry

LPD=Lympho-Proliferative Disorders; TB=Tuberculosis

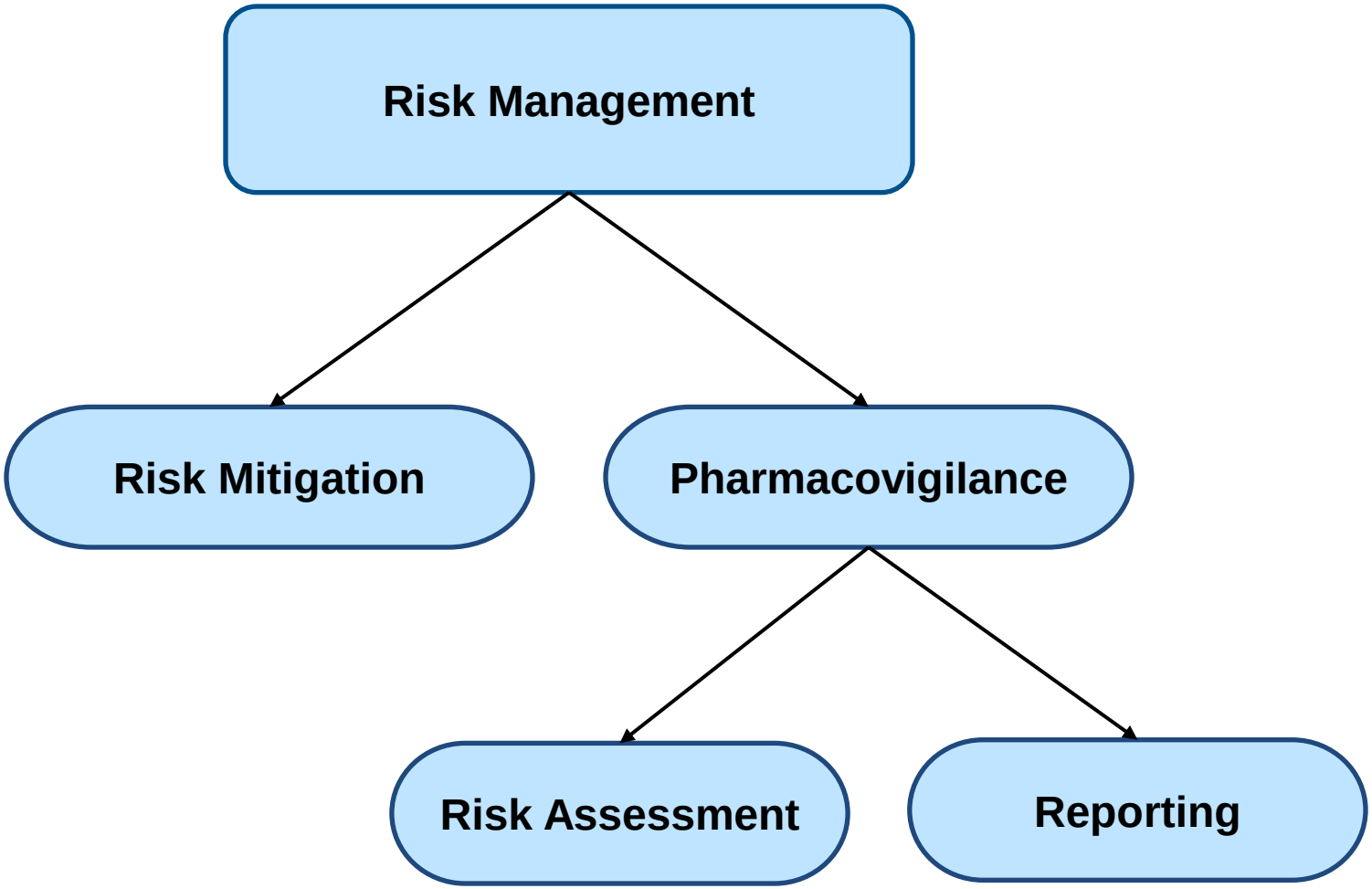
Study 1133 Study Design



- Prospective, Randomized, Open-label, Blinded Endpoint Study (PROBE)
- Phase 3b/4 Event-driven trial (FDA PMR study)
- Co-primary endpoints: MACE and malignancies
- Population: Adults with rheumatoid arthritis
- 4372 subjects randomized
- External Steering Committee
- External DSMB
- Endpoint Adjudication Committees
  - CV, malignancy, hepatic, opportunistic infections, GI perforation, ILD

DSMB=Data and Safety Monitoring Board; ILD=Interstitial Lung Disease; PMR=Postmarketing Requirement

Effective Approach to Risk Management for Tofacitinib



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Benefit:Risk and Conclusions	**Michael Corbo, PhD** **Senior VP, Chief Development Officer** **Inflammation and Immunology** **Pfizer Inc**

Benefit:Risk and Conclusions

Michael Corbo, PhD

Senior VP, Chief Development Officer
Inflammation and Immunology
Pfizer Inc

XELJANZ® (tofacitinib) for PsA
Proposed USPI: Indication and Dosage

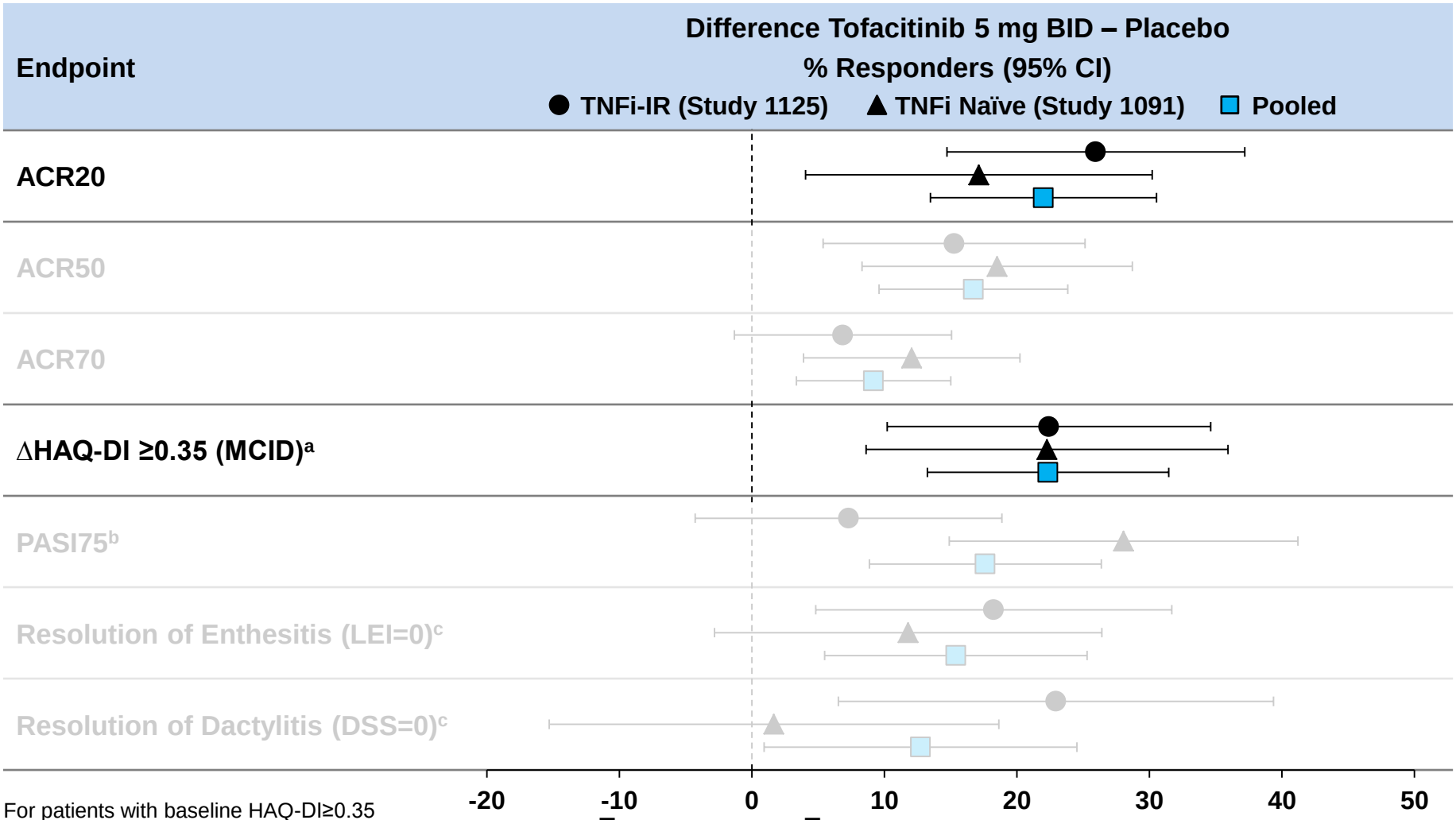
Proposed Indication in sNDA
(1. INDICATIONS AND USAGE)

XELJANZ is indicated for the treatment of adult patients with active psoriatic arthritis

Proposed Dosage in sNDA
(2. DOSAGE AND ADMINISTRATION)

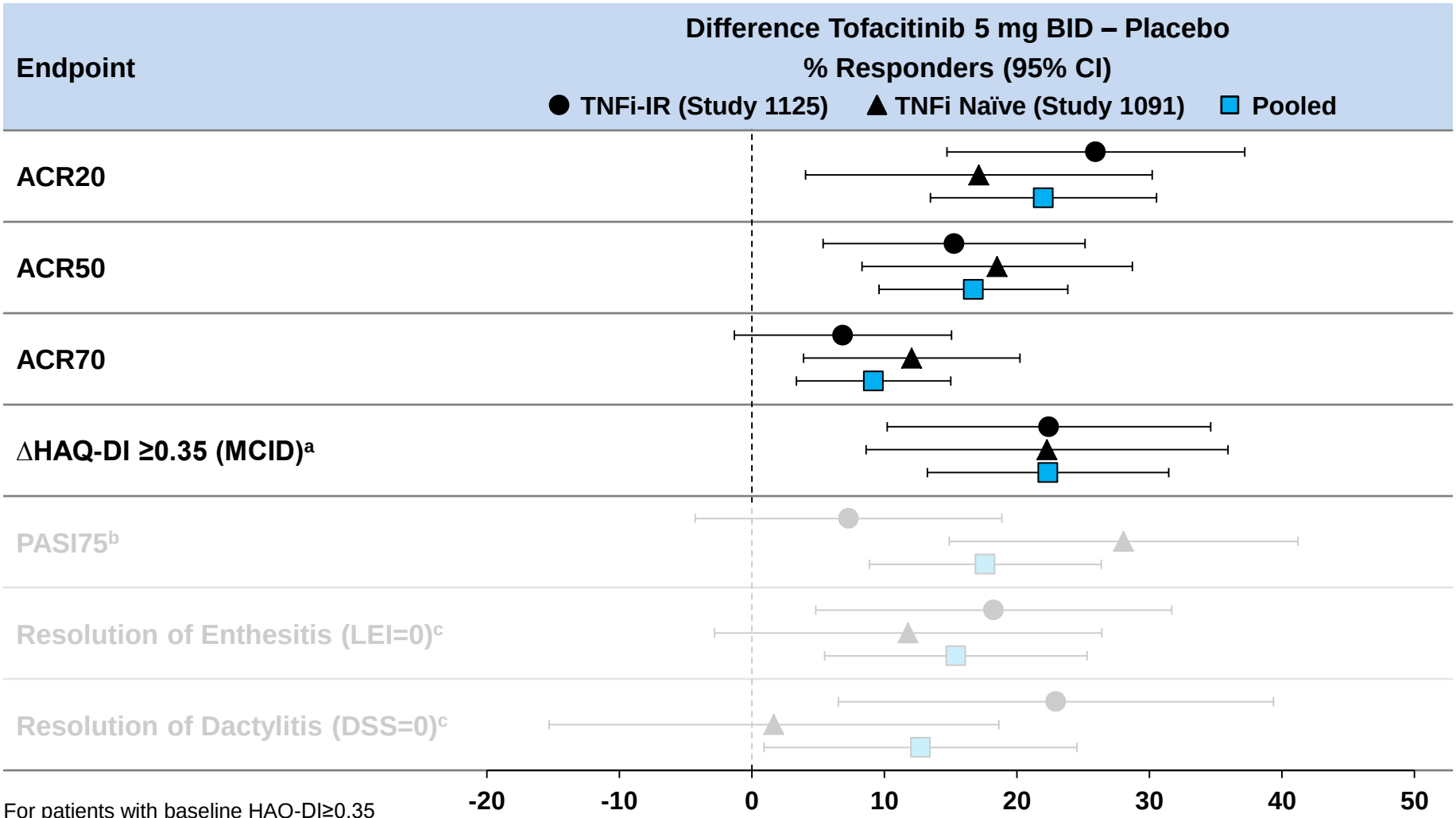
The recommended dose of XELJANZ is 5 mg twice daily used in combination with conventional synthetic DMARDs

Efficacy of Tofacitinib 5 mg BID at Month 3 Across Multiple PsA Manifestations



a. For patients with baseline HAQ-DI≥0.35
b. For patients with baseline BSA≥3% and baseline PASI>0
c. For patients with baseline value>0
MCID=Minimal Clinically Important Difference

Efficacy of Tofacitinib 5 mg BID at Month 3 Across Multiple PsA Manifestations



a. For patients with baseline HAQ-DI≥0.35
b. For patients with baseline BSA≥3% and baseline PASI>0
c. For patients with baseline value>0
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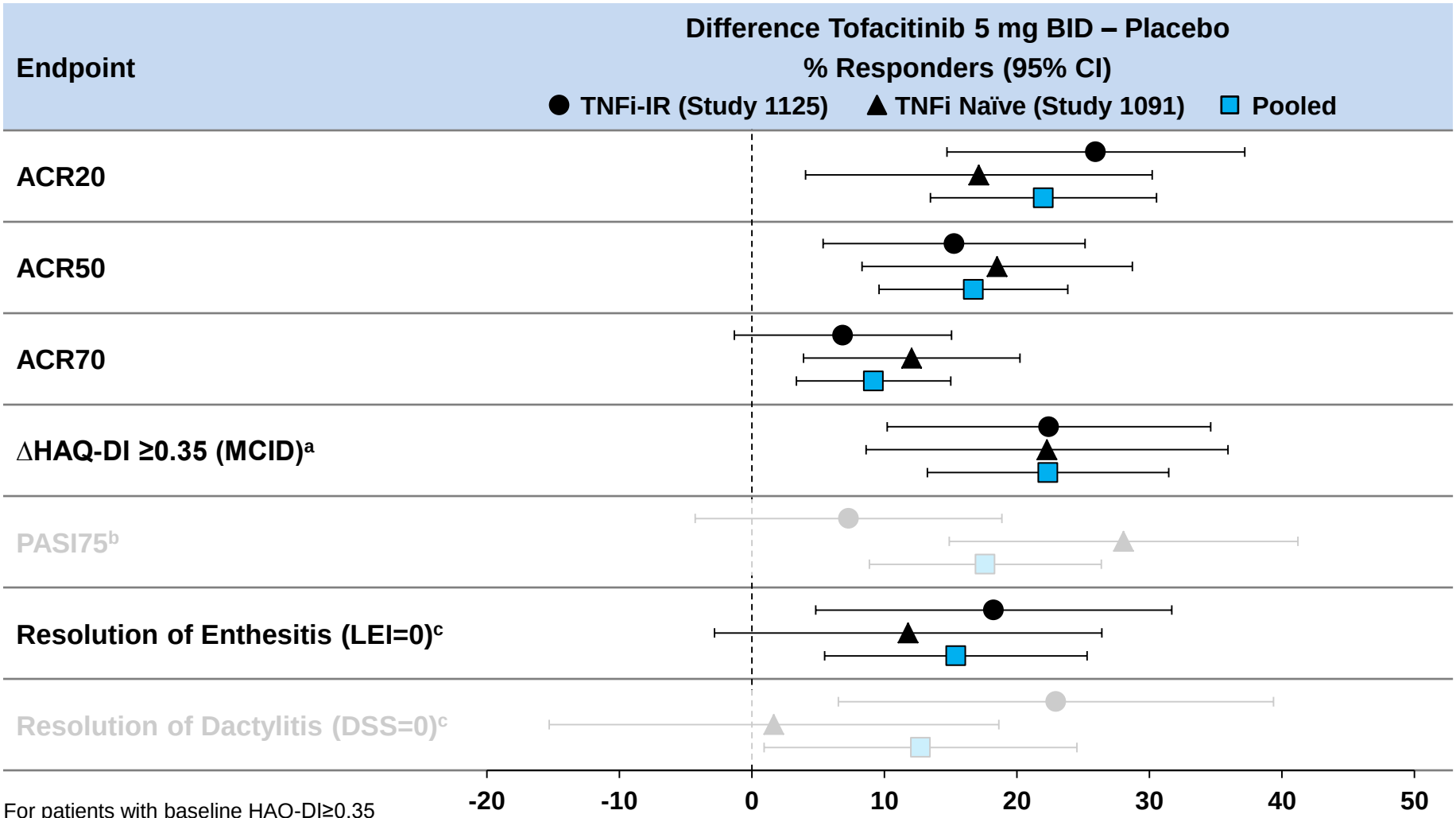
MA-100

Efficacy of Tofacitinib 5 mg BID at Month 3 Across Multiple PsA Manifestations



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MA-101

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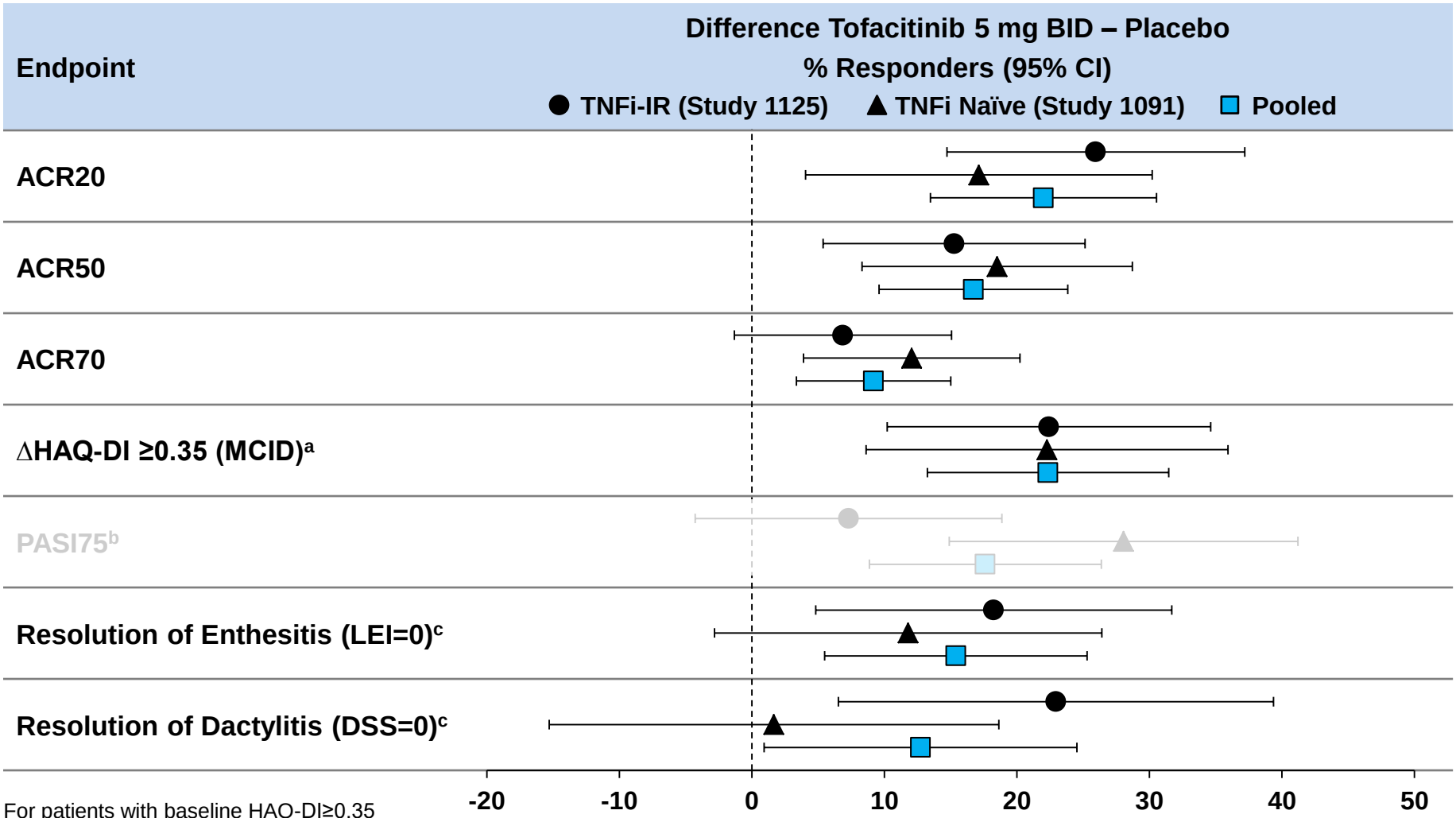

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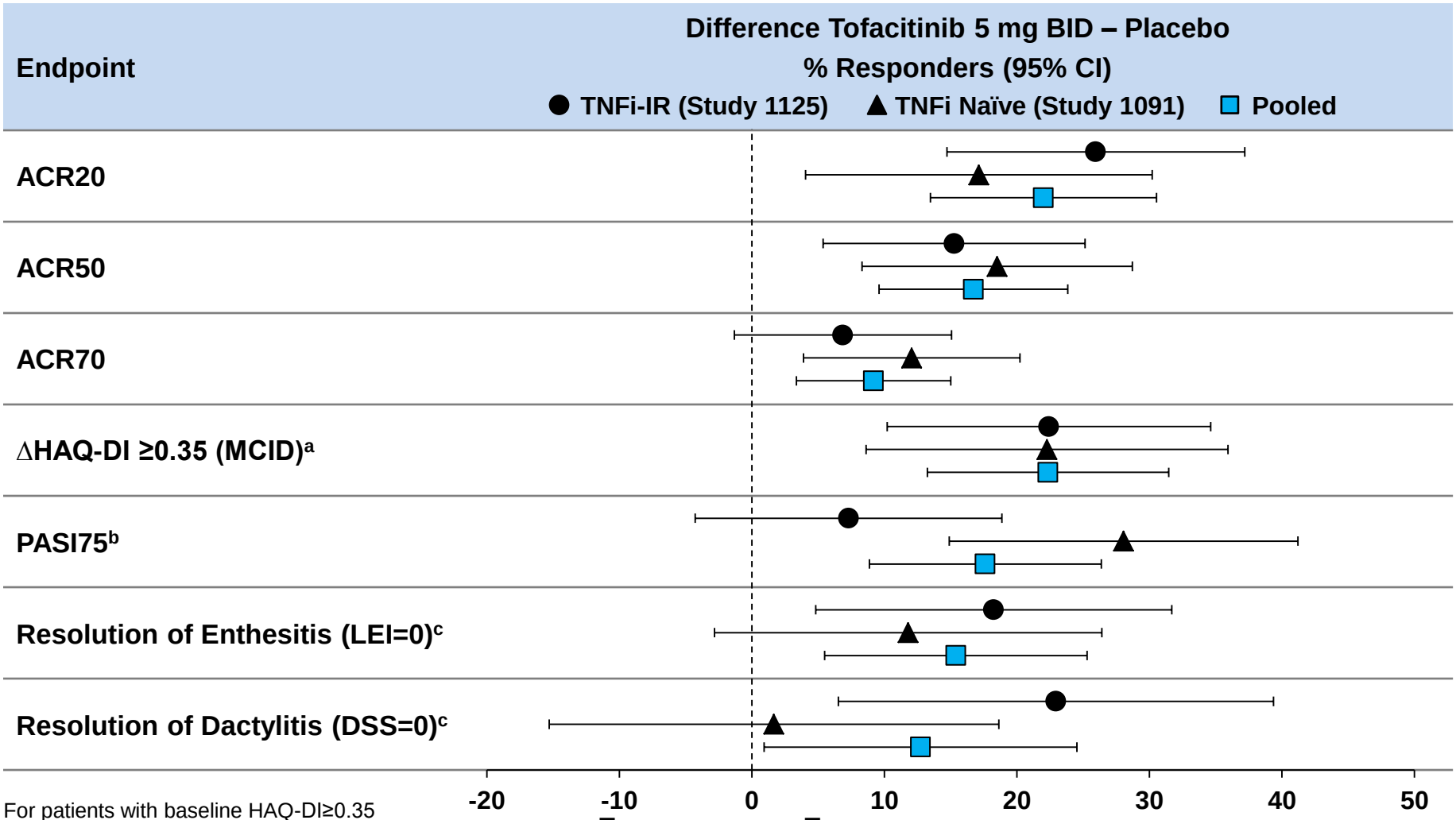

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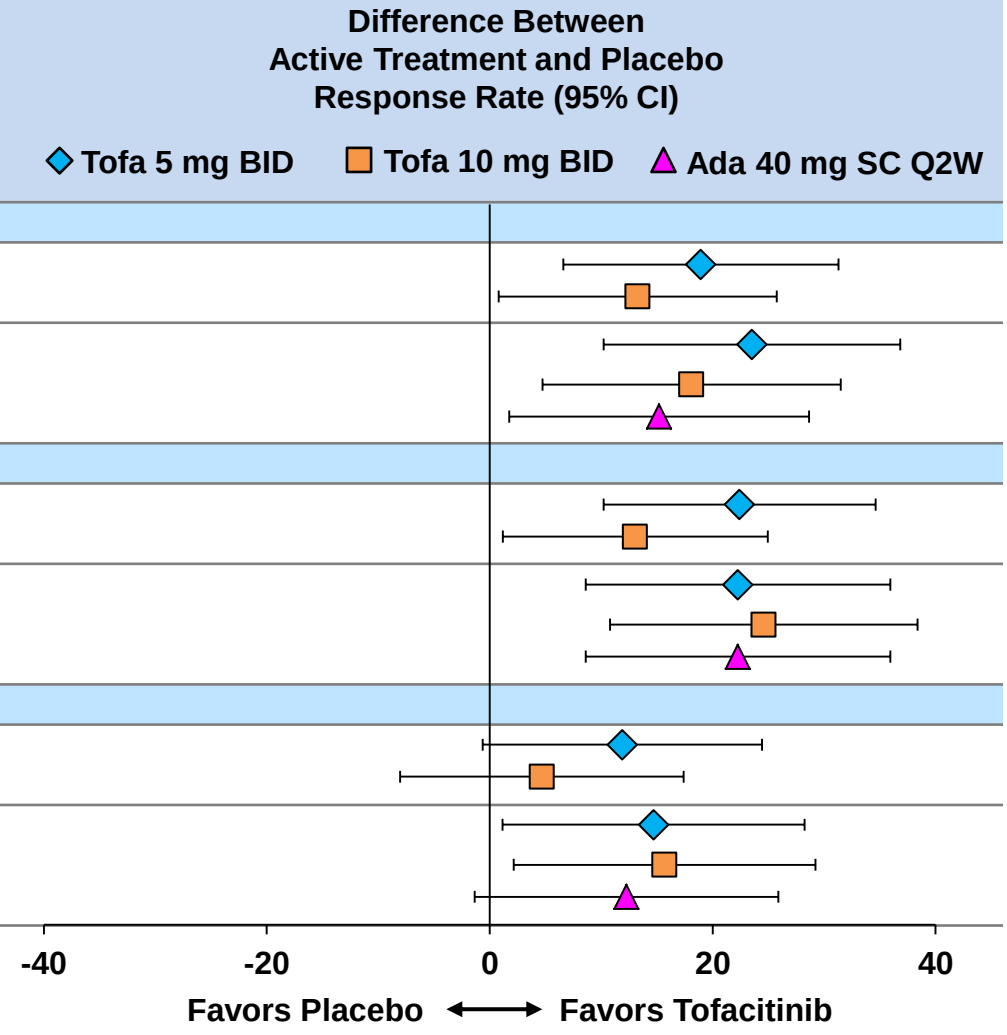
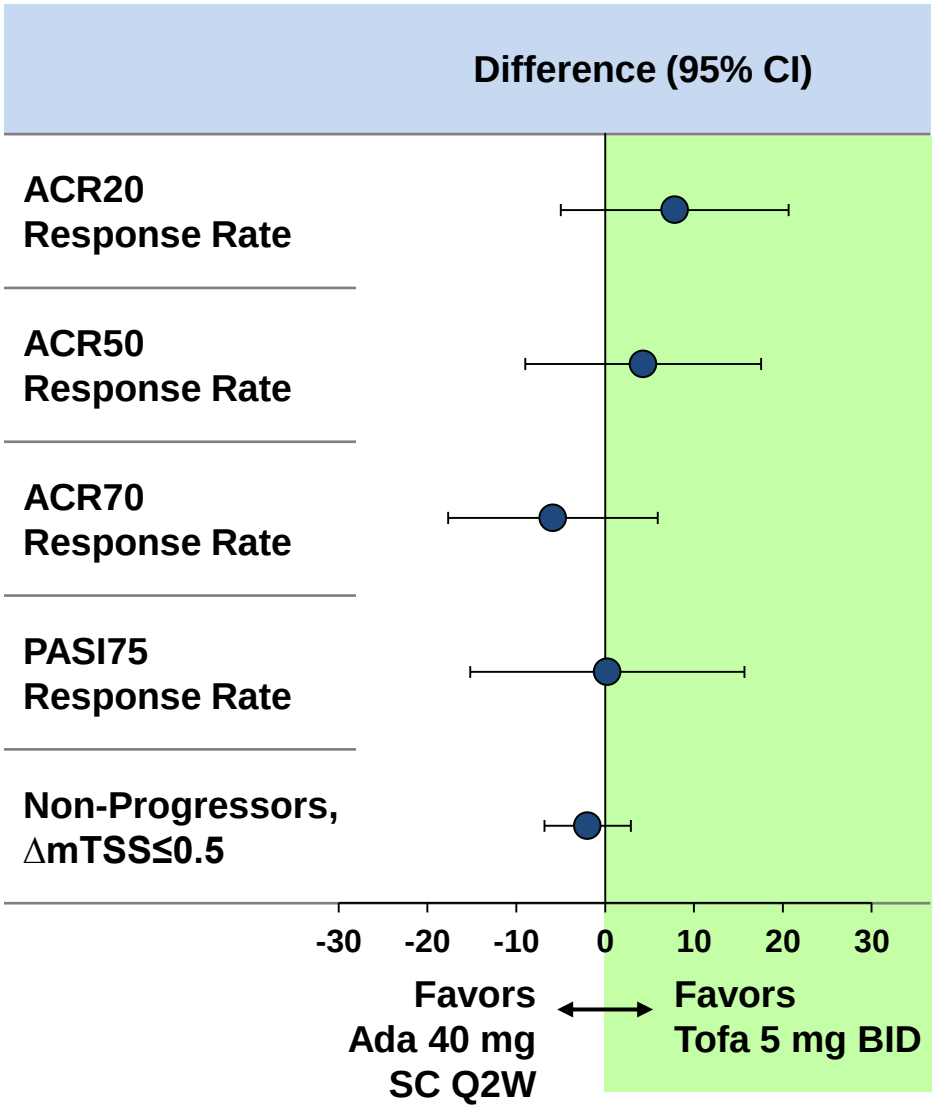
Improvement in Health Related Quality of Life with Tofacitinib at Month 3

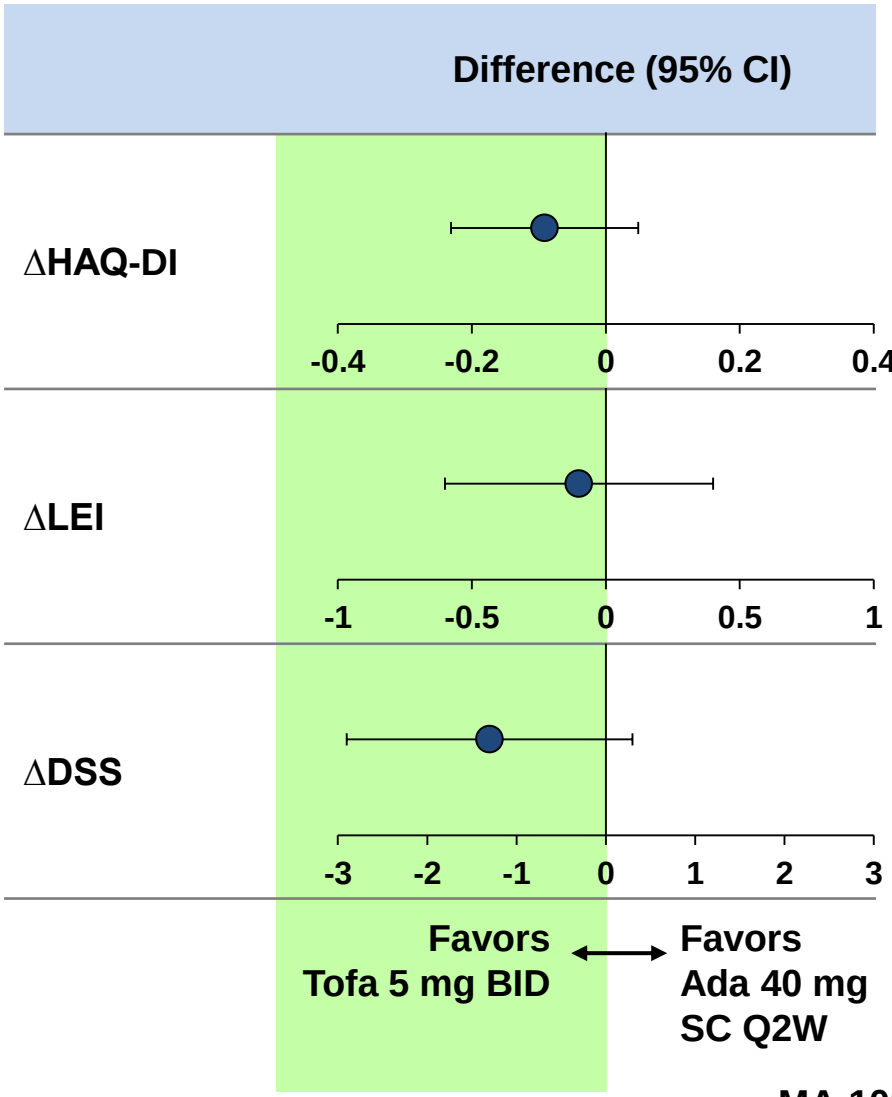
	Active Treatment N	Placebo N
SF-36v2 Physical Functioning Domain (MCID=3.5)		
TNFi-IR (Study 1125)	124	117
	120	117
TNFi Naïve (Study 1091)	102	102
	103	102
	101	102
HAQ-DI (MCID=0.35)		
TNFi-IR (Study 1125)	116	116
	123	116
TNFi Naïve (Study 1091)	96	94
	92	94
	96	94
FACIT-F Total Score (MCID=4)		
TNFi-IR (Study 1125)	124	117
	120	117
TNFi Naïve (Study 1091)	102	102
	102	102
	101	102



Data shown are patients achieving MCID

Comparison Between Tofacitinib 5 mg BID and Adalimumab in TNFi-Naïve Patients (Study 1091) Across Multiple PsA Disease Manifestations (Month 12)



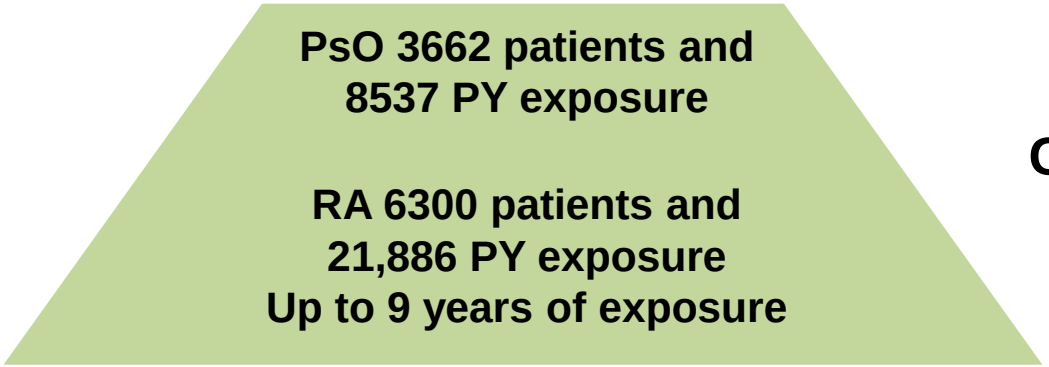


MA-105

Risk Assessment

Foundation of Safety Database for Tofacitinib

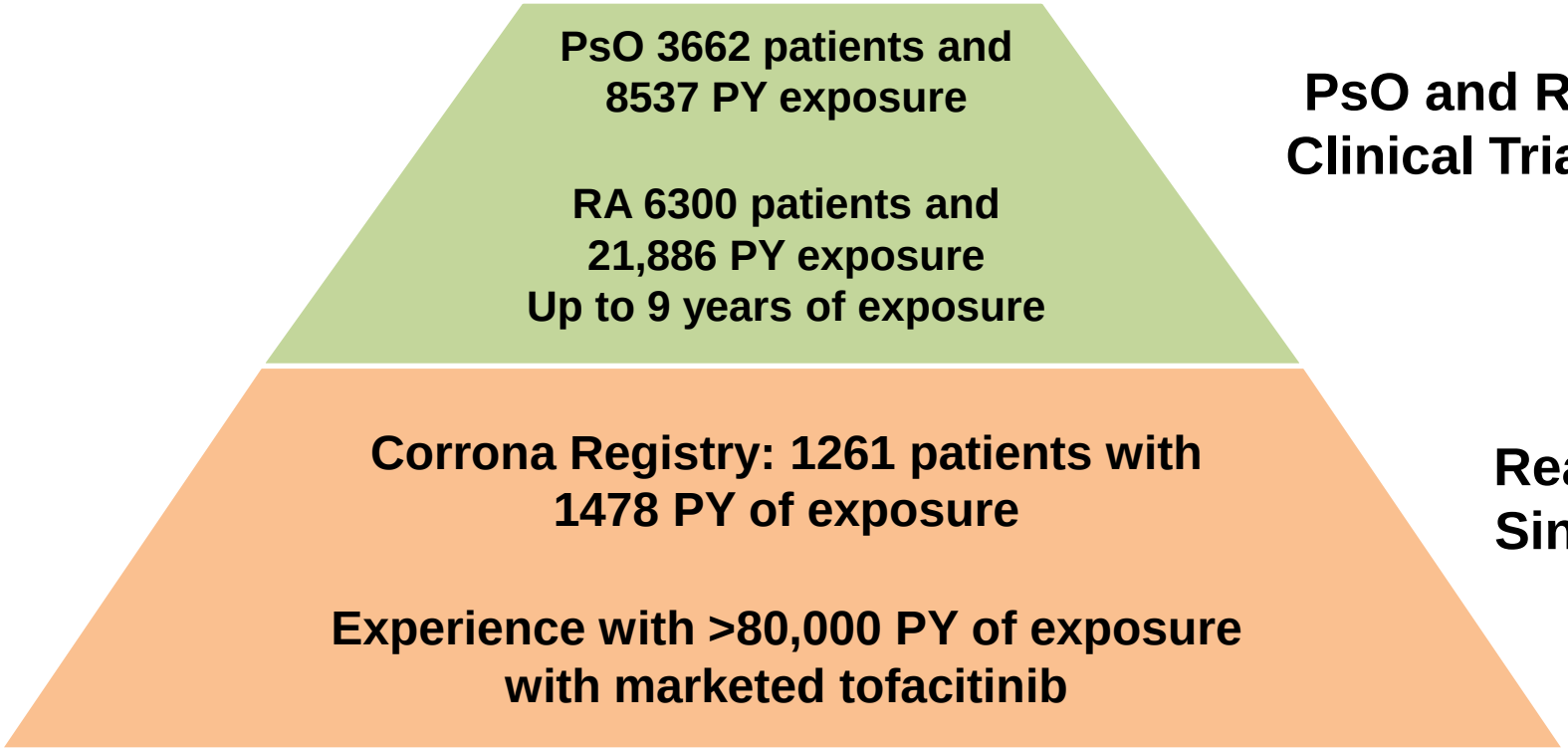
Extent of Exposure in Tofacitinib Development Programs



PsO and RA Clinical Trials

Foundation of Safety Database for Tofacitinib

Extent of Exposure in Tofacitinib Development Programs and Marketed Drug

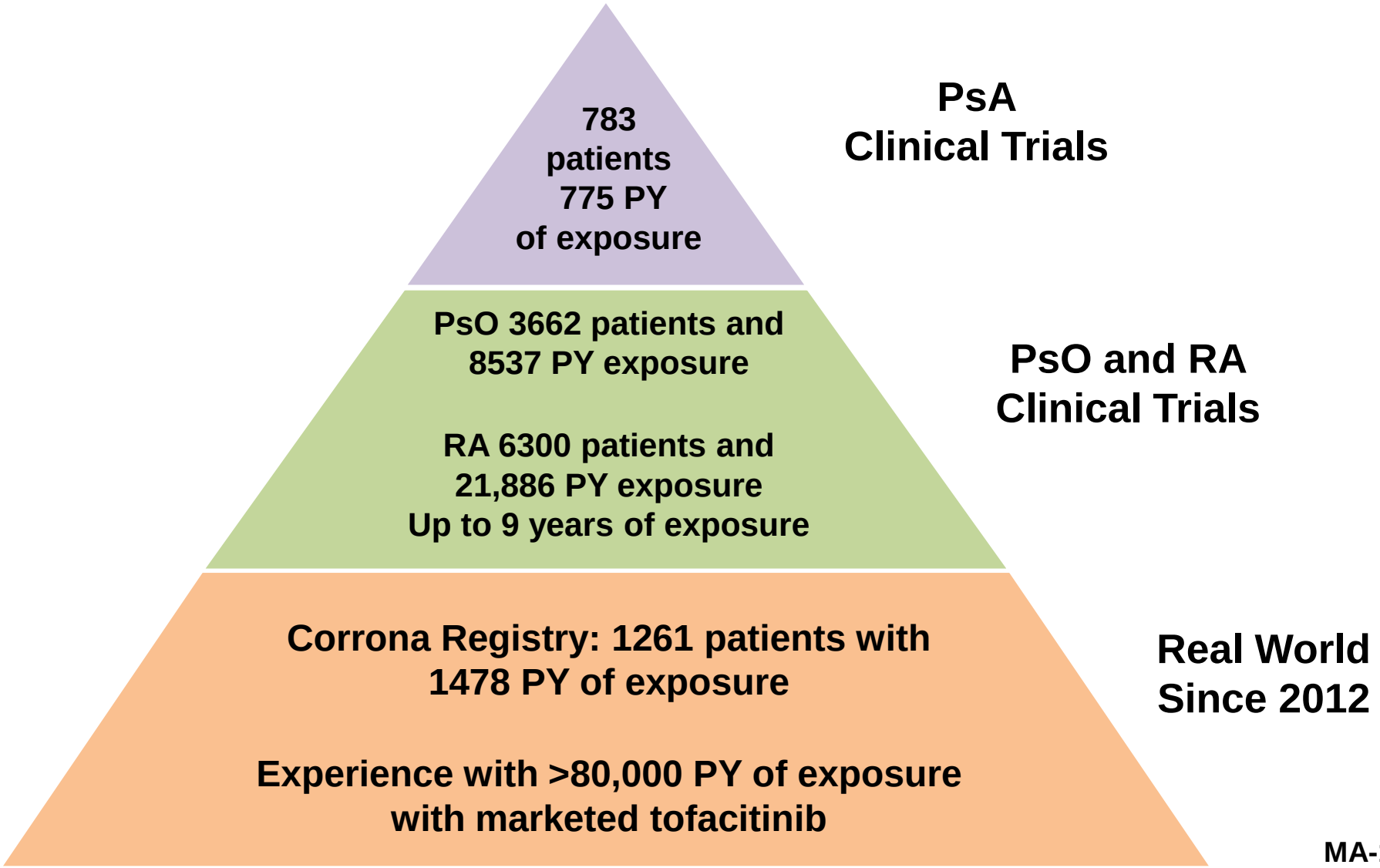


PsO and RA Clinical Trials

Real World Since 2012

Overall Tofacitinib Safety Database

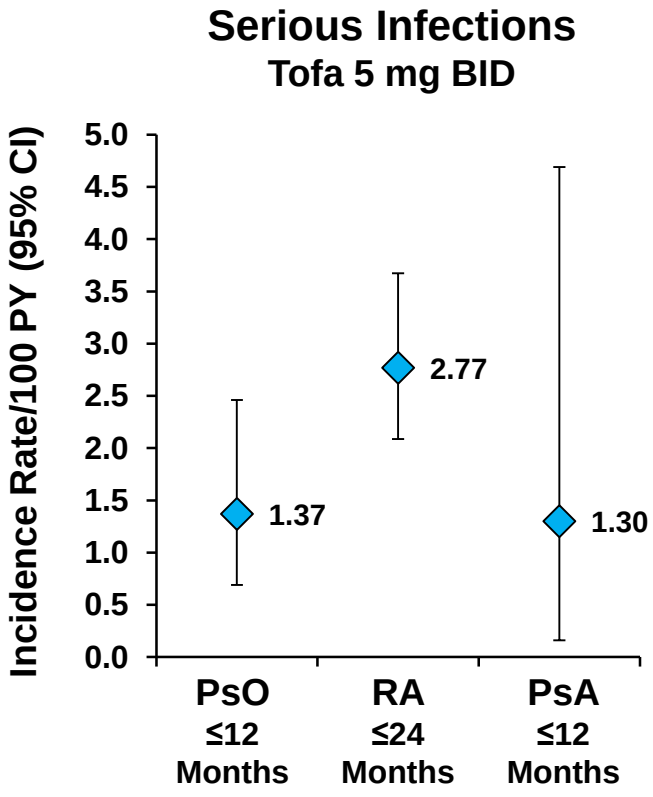
Exposure to Tofacitinib Supporting Safety in PsA



Safety of Tofacitinib 5 mg BID in PsA

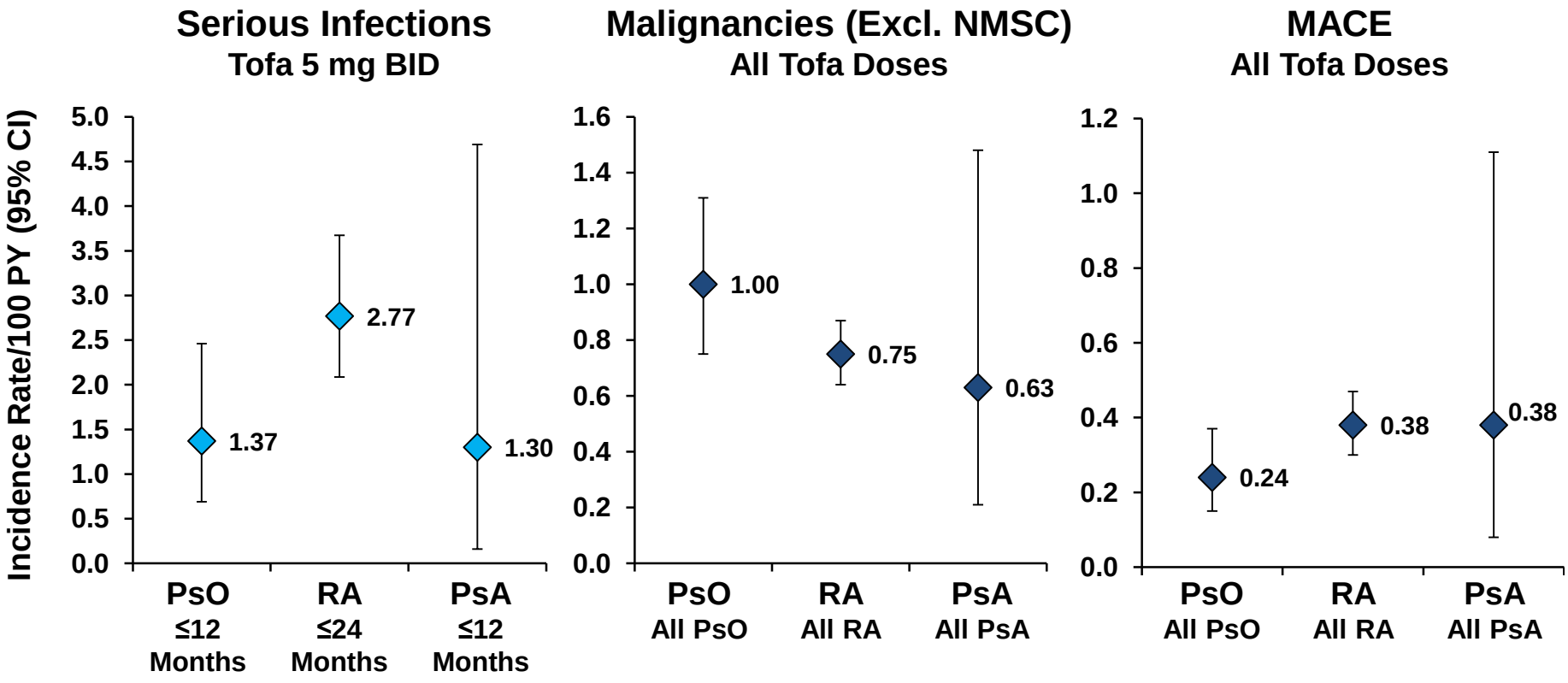
- Infections
  - All
  - Serious
  - Herpes zoster
- Lab Changes
  - Lipids (LDL and HDL)
  - Lymphocytes
  - Transaminase changes
- Non-Melanoma Skin Cancer
- Potential Risks
  - Malignancies excluding NMSC
  - MACE

Risks with Tofacitinib Treatment are Consistent Across Diseases



N	1217	1589	238
n	11	48	2
PY of Exposure	800.8	1733.8	154.1

Risks with Tofacitinib Treatment are Consistent Across Diseases

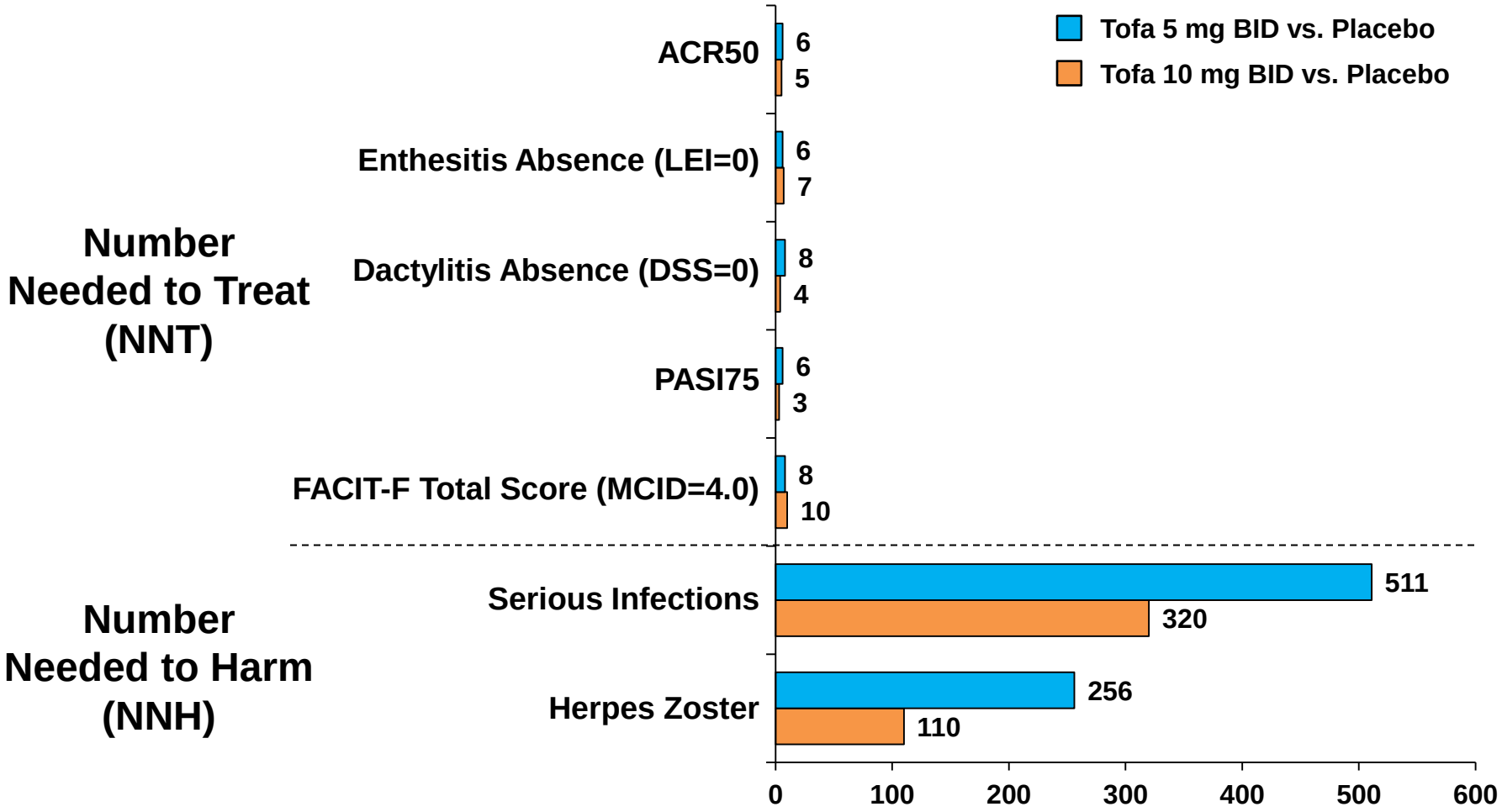


N	1217	1589	238	3623	6300	783	3662	5856	783
n	11	48	2	52	168	5	21	80	3
PY of Exposure	800.8	1733.8	154.1	5203.6	22,353.7	790.5	8759.3	21,285.9	790.5

Scope and Effectiveness of Risk Management of Tofacitinib

- Overlapping risks with RA
- Proven signal detection/assessment/reporting
- Addition of PsA-specific measures including
  - Labeling
  - Long term safety assessment in clinical trial setting up to 4 years
    - More detailed understanding of long-term events in PsA

NNT/NNH for Tofacitinib 5 and 10 mg BID vs. Placebo at Month 3



NNT (efficacy)/NNH (safety) is defined as the inverse of the proportion difference between active treatment group and placebo adjusting for study effect in PsA trials (NNT) or adjusting for RA, PsO and PsA indications (NNH) using Cochran-Mantel-Haenszel weighted approach

Tofacitinib: Favorable Benefit:Risk in the Treatment of PsA Patients

Benefits

Clinical effect across key manifestations

PRO=Patient Reported Outcome

Tofacitinib: Favorable Benefit:Risk in the Treatment of PsA Patients

Benefits

Clinical effect across key manifestations

Efficacy in csDMARD IR and anti-TNF IR

PRO=Patient Reported Outcome

Tofacitinib: Favorable Benefit:Risk in the Treatment of PsA Patients

Benefits

- **Clinical effect across key manifestations**
- **Efficacy in csDMARD IR and anti-TNF IR**
- **Effects demonstrated as early as 2 weeks**

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- **Oral, small molecule without anti-drug antibody formation**

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- Oral, small molecule without anti-drug antibody formation
- Positive results across suite of PROs at the population and patient level

Risks

Examples of events include infections, herpes zoster, NMSC and malignancies (excluding NMSC)

Consistent with RA safety profile
Addressed through established Risk Management
Further informed by long-term studies

PRO=Patient Reported Outcome

Backup Slides Shown

Baseline Methotrexate Dose in TNFi-Naïve Patient Population (Study 1091)

	Placebo N=92		Tofa 5 mg BID N=92		Tofa 10 mg BID N=92		Ada 40 mg SC Q2W N=79	
	Mean (SD)	Median (Range)	Mean (SD)	Median (Range)	Mean (SD)	Median (Range)	Mean (SD)	Median (Range)
Baseline MTX dose, mg/week	15.5 (4.12)	15.0 (5-20)	16.4 (3.79)	15.0 (10-25)	16.8 (11.7)	15.0 (5-105)	15.8 (4.44)	15.0 (5-25)

Dose of MTX 105 mg/week is data error

Immune Response to LZV in Zoster Vaccine Study 1237 in RA Patients

- RA patients starting Tofacitinib 5 mg BID had similar VZV-specific humoral and cell-mediated immune responses to LZV as compared to placebo-treated patients

Immunogenicity assessment	Study 1237	
	Tofa 5 mg BID	Placebo
Change in VZV IgG at week 6 (IgG fold-rise)	2.11 fold rise 80% CI=(1.87, 2.37)	1.74 fold rise 80% CI=(1.55, 1.95)
Absolute Value of VZV IgG titer at week 6 (ELISA Units/mL)	Baseline: 201 Week 6: 403	Baseline: 182 Week 6: 323
Change in VZV ELISPOT at week 6 (SFC fold-rise) (SFCs/10^6 PBMCs)	1.5 80% CI=(1.31, 1.70)	1.29 80% CI=(1.14, 1.46)
Absolute Value of VZV SFCs/10^6 PBMCs	Baseline: 48 Week 6: 70	Baseline: 43 Week 6: 56

ELISA=Enzyme-Linked Immunosorbent Assay; ELISPOT=Enzyme-Linked ImmunoSpot; LZV=Live Zoster Vaccine; PBMC=Peripheral Blood Mononuclear Cell; SFC=Spot Forming Cells; VZV=Varicella Zoster Virus